VOLUME 78 • NOVEMBER 1958 • NUMBER 5

A.M.A. ARCHIVES OF DERMATOLOGY

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Control of Emotional Factors in Dermatoses
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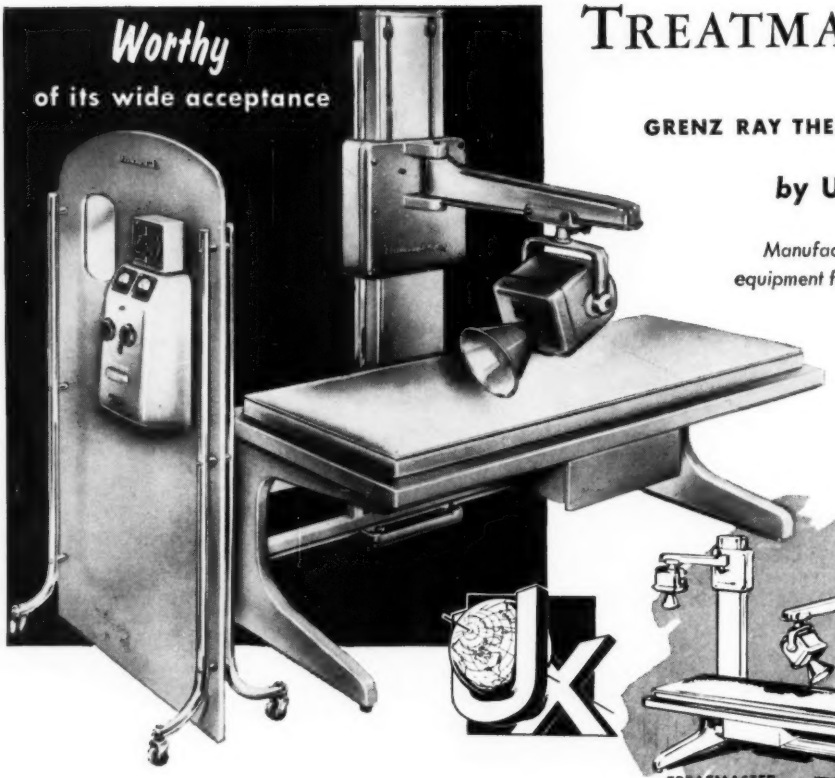

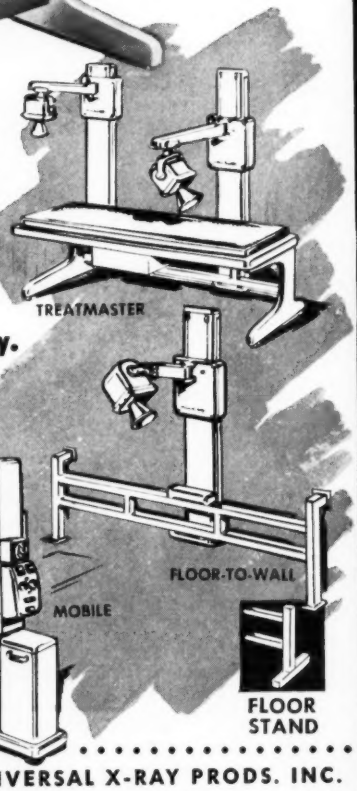

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AMERICAN MEDICAL ASSOCIATION Publication

Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee. Second-class mail privileges authorized at Nashville, Tenn., Aug. 6, 1956.

CHANGE OF ADDRESS: When there is a change of address, the Circulation Office of the American Medical Association should be notified at least six weeks before the change is made. The address label clipped from the subscriber's latest copy of the publication and a statement of old and new address should be included. If there is a postal zone number, it too should be included in the new address. The instructions should state whether the change is permanent or temporary.

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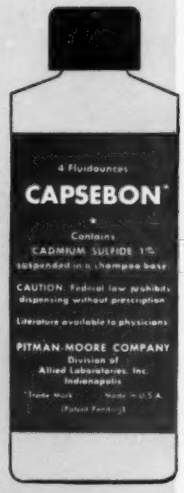

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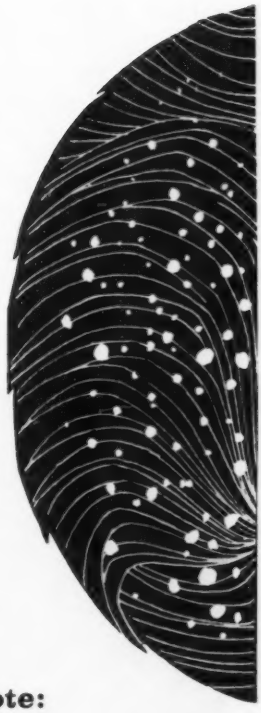

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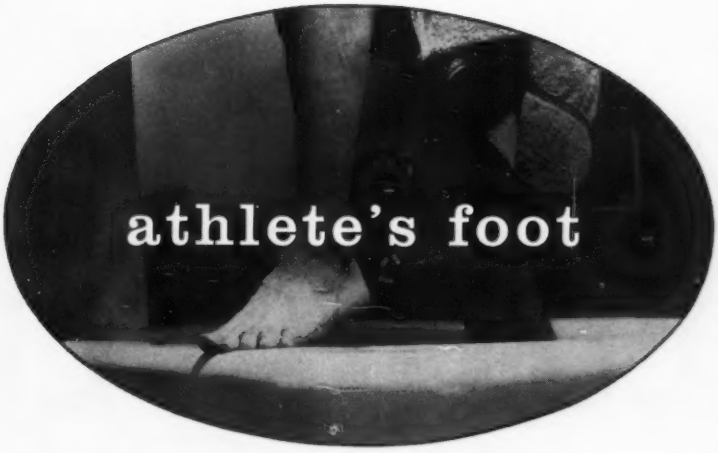

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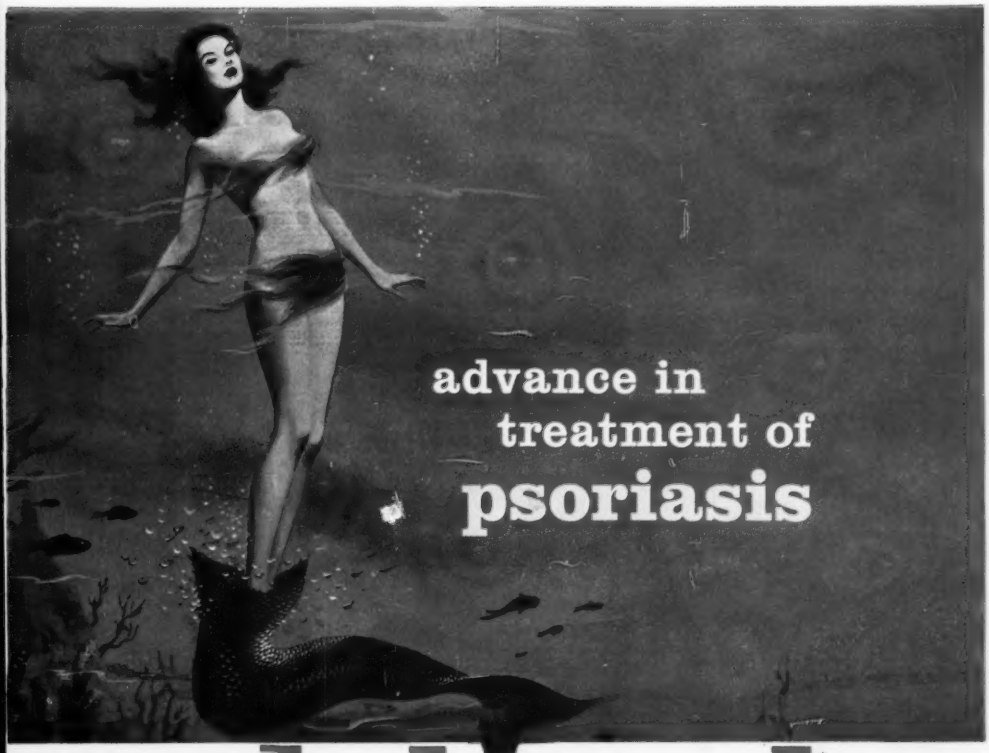

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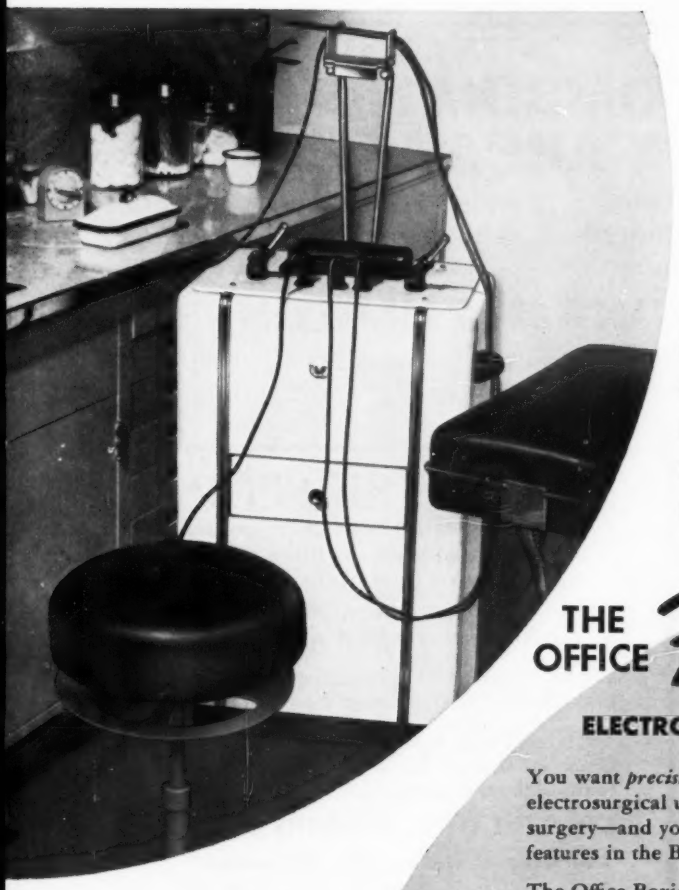

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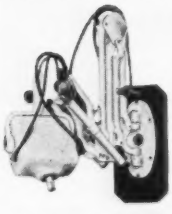

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Dryness of the skin from fluid loss is the vital factor in housewife's eczema. Many preparations used for treatment of such cases further irritate the skin. Barrier creams produce a water-tight "seal" that impedes fluid exchange, with resultant maceration or excessive dryness. POLYSORB HYDRATE is a water-in-oil emulsion, analogous to the modern concept of normal skin. Its water fraction is readily released, ensuring prompt relief of the characteristic skin dryness. And the oil phase prevents further moisture loss through the fissured skin. Optimal water balance, once reached, is maintained by the hydrophilic properties of POLYSORB HYDRATE.

POLYSORB HYDRATE is bland, nonsensitizing and nonirritating. It is not a barrier or steroid preparation.

Available in 50-gram tubes. POLYSORB HYDRATE is a water-hydrated, specially processed, balanced emulsion system consisting of sorbitan sesquioleate and wax petrolatum.

FOUGERA E. FOUGERA & COMPANY, INC.
75 Varick Street, New York 13, N. Y.

breaking the tolerance barrier in dermatoses

new

HYDRO-TAR™

Cream

(Liquor Carbonis Detergens with Hydrocortisone, ALMAY)

takes the "sting" out of coal tar . . .
adds corrective action to hydrocortisone.

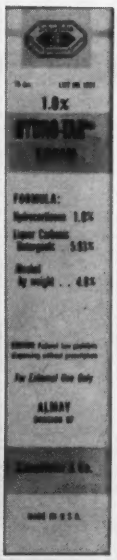
HYDRO-TAR suppresses dermatoses with triple action: antipruritic, antieczematic, and anti-inflammatory. It affords seven important advantages in clinical usage:

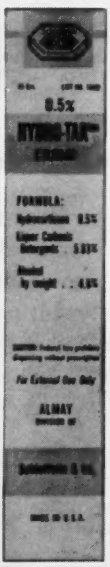
1. Greatly improved toleration of coal tar.
2. Broader scope of application.
3. Rapid responses.
4. Liquor Carbonis Detergens . . . advanced coal tar compounds.
5. Hydrocortisone . . . superior anti-inflammatory agent.
6. Superior cream base.
7. Flexibility of dosage . . . 0.5% and 1.0%.

Dosage: Apply topically by gentle massage to affected areas 3 or 4 times a day . . .

0.5% for moderately severe dermatoses or maintenance–1.0%. for severe dermatoses.

Supplied: 15 gm Tubes in 0.5% and 1.0% strengths.





Samples and literature sent on request.

Schieffelin & Co./Since 1794

ALMAY DIVISION
22 Cooper Square, New York 3, N. Y.

with four-way regression of Acne lesions.

For the acne sufferer, RESULIN-F provides the mutual potentiating effects of (1) resorcin, (2) sulfur, and (3) hydrocortisone; NEO-RESULIN-F adds (4) neomycin to give antibiotic action when infection is present or must be prevented.

The resulting broadside of therapeutic actions expedites regression of the acne lesions. Its chief effects are: dehydrative, antiseborrheic, moderately exfoliative, anti-pruritic, anti-inflammatory, anti-allergic, fungistatic, parasitic, antibacterial, and preventive against follicular hyperkeratosis.

Toleration is excellent, and both preparations have superior dermal penetrability. Their striking effectiveness has been shown even in cases that resisted other forms of therapy.

Dosage: Apply 3 times daily to lesions and adjacent areas.

Supplied: In 15 Gm. tubes.

Samples and literature available on request.

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ALMAY DIVISION

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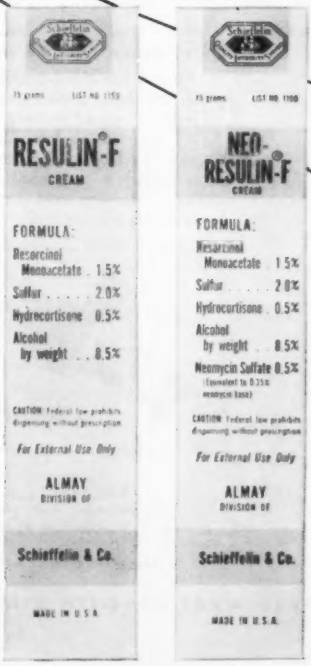


FRIGIDERM®

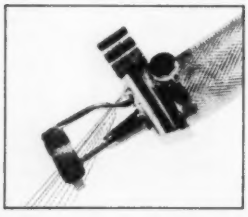
(100% dichloro-tetrafluoro-ethane...contains no ethyl-chloride)

SKIN REFRIGERANT–ANESTHETIC

*Widely Accepted for Local Anesthesia in Surgical Planing of the Skin**

JET-SPRAY PLANER

This hand-tooled, precision-built instrument with diamond fraises is available for most standard planing units. In ordering, please specify make of planing unit. Full information on request.



FRIGIDERM has been researched and developed to meet the expressed need of physicians for a well tolerated skin refrigerant-anesthetic...non-explosive, non-inflammable...having no general anesthetic properties.

Today, **FRIGIDERM** is one of the preferred products of its kind among Dermatologists everywhere.

FRIGIDERM quickly produces local anesthesia for surgical planing in the treatment of scarring due to acne, chickenpox, smallpox and trauma...multiple senile keratoses...fine wrinkling...traumatic tattoos.

Also for incision of furuncles, electrocautery to small cutaneous tags, flat warts, or for alleviation of needle pain during hypodermic injection.

This freezing agent can be delivered from the spray-top container shown above by easy finger pressure.

Now in the improved 8 oz. container — $2.00

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**A.M.A. Archives of Dermatology, April 1955*
Ref.: Wilson, J. W.; Luikari II, R.; Ayres III, S., Reprints available

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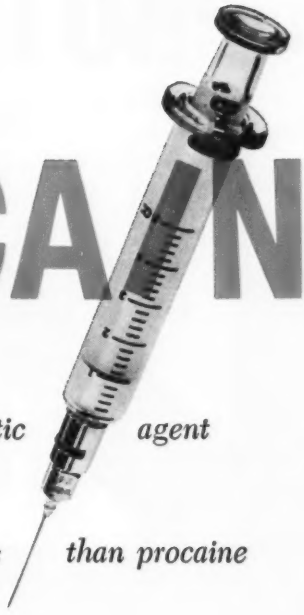
NESACAINE®

(CHLOROPROCAINE HYDROCHLORIDE)



the new local anesthetic agent

more potent . . . yet no more toxic than procaine

SWIFT ONSET "Sensory anesthesia was complete within 6 to 10 minutes."[1]

NOTABLE SAFETY The chief virtue of Nesacaine appears to be its relatively low toxicity — no reactions in 350 anesthetics.[2]

HIGH DIFFUSIBILITY "The almost instantaneous onset of anesthesia . . . is caused by the increased penetrating capacity [of Nesacaine] . . ."[3]

MAXIMAL EFFICACY "Nesacaine . . . was found effective . . . it would appear to be [an agent of choice] for use as a local anesthetic."[2]

1. Colavincenzo, J. W., and others: Pennsylvania M. J. 59:338 (March) 1956.
2. Ansbro, F. P., and Furlong, R. E.: Adelphi Hosp. Bull. 15:2 (May) 1957.
3. Foldes, F. F., and McNall, P. G.: Anesthesiology 13:287 (May) 1952.

In 30 cc multiple dose vials—

1% Nesacaine for infiltration and field block
2% Nesacaine for regional block

In 30 cc single dose vials—

3% Nesacaine for caudal and epidural block

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TO PROTECT SKIN

AGAINST A WIDE RANGE OF IRRITANTS

- *in industry*
- *in the home*

Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

SUGGESTED DOSAGE: Cleanse area thoroughly with soap and water. Apply thin film as required and rub in well. If skin is exposed constantly to irritant, apply every 2-4 hours, or as needed to provide protection. It is not necessary to remove original coat before applying subsequent coats. Any objectionable greasiness may be removed by wiping with a dry cloth, or washing gently with soap and water.

CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
Industrial Dermatoses
Chapping—Chafing
Intertrigo
Diaper Rash
Chronic Dermatoses
Aggravated by Soap and Water

SILICOTE CONTAINS
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble ingredients.

Send for samples and literature

1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

SILICOTE
SILICONE OINTMENT

ARNAR-STONE LABORATORIES, INC. **MT. PROSPECT, ILLINOIS**

In Canada: Brent Laboratories, Ltd., Toronto

CONTROL EMOTIONAL FLARE-UPS

that cause or aggravate SKIN ERUPTIONS

Miltown®

meprobamate (Wallace)

In neurodermatitis, atopic dermatitis, chronic urticaria, eczematoid dermatitis, lichen planus, psoriasis, pruritus ani, pruritus vulvae

Eighty per cent of 224 patients with a wide variety of skin disorders responded favorably to adjunctive therapy with Miltown.[2]

"is an effective addition to conventional dermatological therapy."[1]

- relieves anxiety and tension with exceptional safety
- suitable for prolonged administration
- does not impair physical efficiency or mental alertness

References: 1. Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. **74**:393, Oct. 1956. 2. LeVan, P.: Clinical dermatologic studies of four chemically different tranquilizers. Clinical Med. **4**:1089, Sept. 1957.

Literature and samples on request

WALLACE LABORATORIES, *New Brunswick, N. J.*

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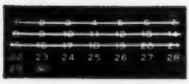
RAPID HEALING...3 WEEKS



for PRURITUS ANI

orally treated with ....Borcherdt

MALT SOUP EXTRACT

More and more physicians are telling us of the successful results from treating Pruritus Ani orally with Borcherdt's Malt Soup Extract. The intractable itching disappears in three or four days and the perianal skin becomes normal in three or four weeks. Even stubborn cases of many years standing usually yield or show marked improvement.

Malt Soup Extract is a non-diastatic barley malt extract neutralized with potassium carbonate. Most importantly, it promotes aciduric bacteria in the lower intestine, creates easily passed stools and overcomes, in a natural way, the alkaline condition so prevalent in cases of Pruritus Ani.

There are no side effects; no drug fastness, no gas pain. Malt Soup Extract is a food not a drug. Results are secured naturally and once attained medication can be discontinued or greatly reduced.

Malt Soup Extract is available in 8 and 16 ounce jars at most pharmacies coast to coast.

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Therapeutic Gloves

save
time
and
motion
where
wet packs
are
required...

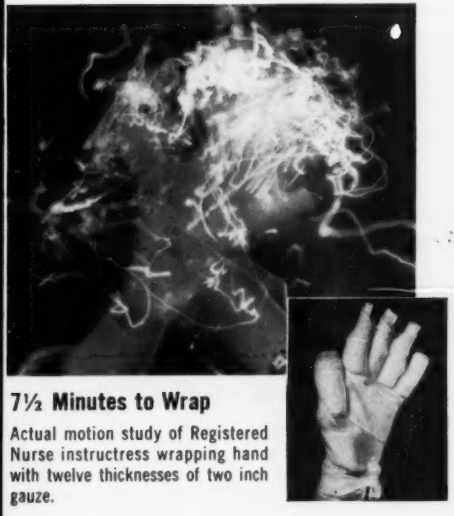
For a time-saving and convenient method of wet compress therapy dermatologists are turning to DERMPAK Therapeutic Gloves when treating eczematous processes of the hands.

DERMPAK Gloves are widely accepted because they not only conserve valuable personnel time but meet with exceptional acceptance by the patient.

DERMPAK Gloves are made of 12-ply quilted hospital gauze . . . sterilized before packaging. They are durable and may be washed and re-used many times.

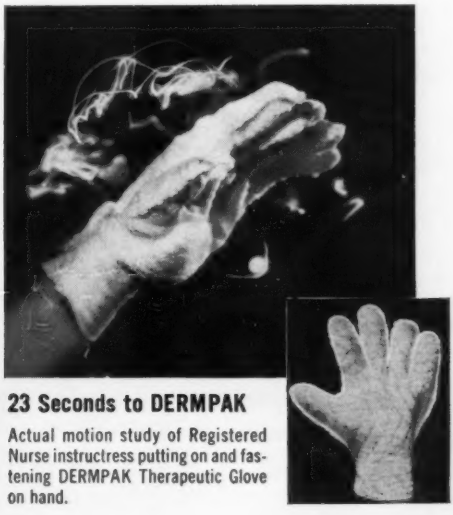
Available, one pair to a sealed package, in small, medium or large sizes.

A free sample glove will be sent on request.



7½ Minutes to Wrap

Actual motion study of Registered Nurse instructress wrapping hand with twelve thicknesses of two inch gauze.



23 Seconds to DERMPAK

Actual motion study of Registered Nurse instructress putting on and fastening DERMPAK Therapeutic Glove on hand.

DERMPAK CORPORATION
282 East 5th Street • St. Paul, Minnesota

Manufactured and distributed under license from the Minnesota Dermatological Society.

CORTROPHIN-ZINC

in Allergies

(Corticotropin-Alpha Zinc Hydroxide)

Description: The new electrolytic Cortrophin-Zinc is indicated in most allergic manifestations. Pollen, drug and food reactions, as well as toxic plant dermatoses are significantly improved. Because of prolonged activity, frequent injections are not necessary. Each injection is effective for at least 24 hours, and in milder cases, for 72 hours.

Characteristics: New Cortrophin-Zinc provides corticotropin of unsurpassed purity with low foreign protein content. This reduces the risk of sensitization reactions.

Since about 5% of the corticotropin is uncombined, onset of clinical response is rapid. But the balance, present as a complex of alpha zinc hydroxide, provides a prolonged action so that the effective time span of a single dose is usually several days. Injection of the new electrolytic Cortrophin-Zinc is virtually painless.

Pharmacology: A potent stimulator of cortical activity, Cortrophin-Zinc *does not depress* functioning of the suprarenal glands. Unlike the corticosteroids, adrenocorticotropic hormone arouses the adrenal glands to produce *natural* steroids in natural proportions. In a 5-year study of patients on ACTH therapy, no case of adrenal *or pituitary* depression or atrophy has been observed.

Because Cortrophin-Zinc is virtually painless on injection and its prolonged action obviates frequent injections, it is now practicable to use Cortrophin-Zinc in most of the indications where formerly reliance has been on corticosteroids. This freedom from apprehension of deleterious depressive effects permits clinical use of valuable hormone therapy on a broader scale than has been possible heretofore.

Clinical Uses and Dosage: The many published reports on the use of Cortrophin-Zinc as well as ACTH in thousands of patients indicate its value in over 100 disorders. Most responsive have been: allergies and hypersensitivities; rheumatoid arthritis, bronchial asthma, serum sickness and inflammatory skin and eye diseases.

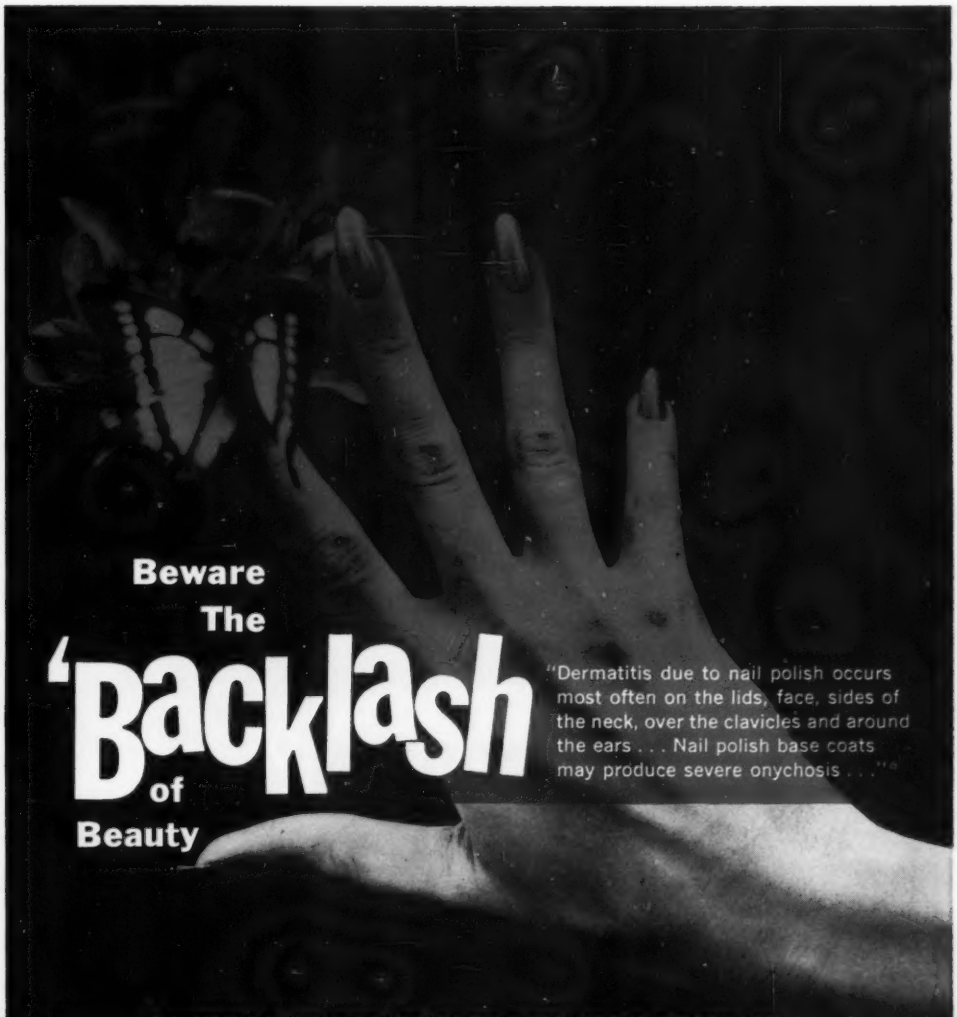
Dosage should be individualized, but generally initial control of symptoms is obtained with a single injection of 40 Units of Cortrophin-Zinc daily until control is evident. Maintenance dosage is generally 20 Units (or less) twice a week.

Use of Cortrophin-Zinc with oral steroids is now recommended as a safety measure to supply the important suprarenal stimulation and lessen the hazard of atrophy. The periodic use of Cortrophin-Zinc is advocated with all steroid analogs, such as cortisone, hydrocortisone, prednisone, prednisolone, methylprednisone and triamcinolone.*

Supply: 5-cc vials containing 40 and 20 U.S.P. Units of corticotropin per cc; 1-cc ampuls containing 40 and 20 U.S.P. Units of corticotropin, with sterile disposable syringes.

*Write for complete literature and bibliography containing specific dosage schedules to:

Medical Department
ORGANON INC. · Orange, N. J.



Beware The 'Backlash of Beauty

"Dermatitis due to nail polish occurs most often on the lids, face, sides of the neck, over the clavicles and around the ears . . . Nail polish base coats may produce severe onychosis . . ."*

Both the dermatitis due to nail polish resin and the eczematous reaction of the nail bed to undercoating can be avoided by using MARCELLE Nail Lacquer without base coat — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

Characteristic of MARCELLE's complete line of hypoallergenic beauty aids — MARCELLE Nail Lacquer is free from known allergens and irritants yet answers the beauty-conscious patient's insistence on cosmetic elegance.

Marcelle COSMETICS, INC.
CHICAGO 47, ILLINOIS

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BORDEN'S Pharmaceutical Division

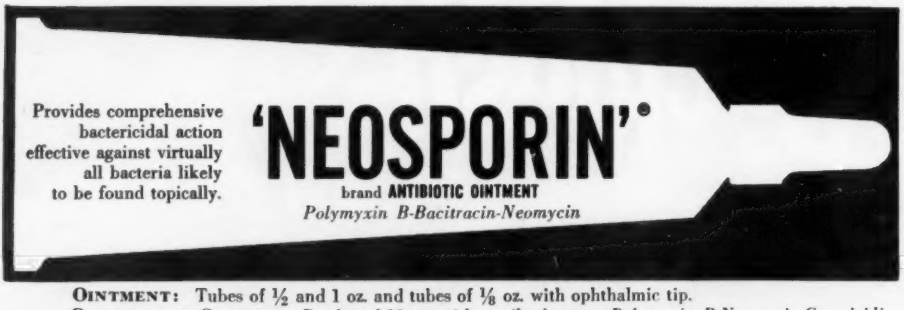
*Andrews, G. C.: Diseases of the Skin, ed. 4, Philadelphia, Saunders, 1954, pp. 117, 118.

For every topical indication, a Burroughs Wellcome 'SPORIN'...

'CORTISPORIN'®
brand OINTMENT
Polymyxin B-Bacitracin-Neomycin with 1% Hydrocortisone
Combines the anti-inflammatory effect of hydrocortisone with the comprehensive bactericidal action of the antibiotics.

OINTMENT: Tubes of ⅛ oz. and ½ oz. (with applicator tip) for ophthalmic or dermatologic application.

OTIC DROPS: Bottles of 5 cc. with sterile dropper. *Polymyxin B-Neomycin with 1% Hydrocortisone*


Provides comprehensive bactericidal action effective against virtually all bacteria likely to be found topically.
'NEOSPORIN'®
brand ANTIBIOTIC OINTMENT
Polymyxin B-Bacitracin-Neomycin

OINTMENT: Tubes of ½ and 1 oz. and tubes of ⅛ oz. with ophthalmic tip.

OPHTHALMIC SOLUTION: Bottles of 10 cc. with sterile dropper. *Polymyxin B-Neomycin-Gramicidin*

NEW **LOTION:** Plastic squeeze bottles of 20 cc. *Polymyxin B-Neomycin*

NEW **POWDER:** Shaker-top bottles of 10 Gm. *Polymyxin B-Neomycin-Bacitracin*

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Polymyxin B-Bacitracin
Offers combined antibiotic action for treating conditions due to susceptible organisms amenable to local medication.

OINTMENT: Tubes of ½ oz., 1 oz. and ⅛ oz. (ophthalmic tip).

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N. Y.

PRESCRIPTION

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despite the advent of steroids...

'Pragmatar' remains a basic medication

in many common skin disorders.

- in seborrheic affections (including "cradle cap" and dandruff)
- in subacute and chronic dermatitis
- in eczematous eruptions
- in fungous infections (including "athlete's foot")

Pragmatar* tar-sulfur-salicylic acid

effective, easy to use, possesses
a wide margin of safety

Smith Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off

dermatoses

Kenacort with its unsurpassed antiallergic, anti-inflammatory and antipruritic activity quickly alleviates the itching, erythema, and irritation in most inflammatory skin conditions.

The table shows the effectiveness of relatively small doses of triamcinolone (Kenacort) in the treatment of some common dermatoses.

Summary of Clinical Effects of Triamcinolone on Dermatoses in Fifty-one Patients.[1]

TYPE OF LESION	HELPED, NO.	NOT HELPED, NO.
Chronic eczematous eruptions, including atopy	14	5
Localized neurodermatitis	4	2
Contact dermatitis	6	6
Seborrheic dermatitis	9	0
Alopecia areata	4	1

In psoriasis, Kenacort should be reserved for those patients suffering from acute, extending or severe chronic forms of the disease. The authors report prompt and dramatic relief in 36 of 60 such patients treated with 12-16 mg. per day.

Kenacort is indicated in the treatment of dermatoses, asthma, allergies and arthritis —

KENACORT
Squibb Triamcinolone

with a low incidence of gastric disturbance [1,2,5,8]
without salt and water retention [1,8]
with no potassium loss [4,8]
without unnatural psychic stimulation [1,2,5]
with no adverse effect on blood pressure [1,2,4,5,7]
on a low daily dosage range [1,2,6,7]

Supply: Scored tablets of 1 mg. and 2 mg.—bottles of 50. Scored tablets of 4 mg.—bottles of 30 and 100.

1. Shelley, W.B.; Harun, J.S., and Pillsbury, D.M.: J.A.M.A. *167*:959 (June 21) 1958. 2. Sherwood, H., and Cooke, R.A.: J. Allergy *28*:97 (March) 1957. 3. Boland, E.W.: Geriatrics *13*:190 (March) 1958. 4. Hellman, L., and others: A.M.A. J. Dis. Child. *94*:437 (Oct.) 1957. 5. Hartung, E.F.: J.A.M.A. *167*:973 (June 21) 1958. 6. Feinberg, S.M.; Feinberg, A.R., and Fisherman, E.W.: J.A.M.A. *167*:58 (May 3) 1958. 7. Friedlaender, S., and Friedlaender, A.S.: Antibiotic Med. & Clin. Ther. *5*:315 (May) 1958. 8. Dubois, E.L.: J.A.M.A. *167*:1590 (July 26) 1958.

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NEW topical germicide unsurpassed for broad range activity

BETADINE®

Brand of Povidone-Iodine

kills outright

including resistant staph.

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- Kills by contact a wide variety of microorganisms such as *Bacteria (including tubercule bacillus), Viruses, Fungi, Protozoa.*
- Effective against certain important organisms resistant to topical antibiotics
- Will not lead to the development of resistant strains
- Effective even in the presence of blood, pus or other organic matter
- Color can be washed off with water.

Available: Betadine Antiseptic in 8 oz. and 16 oz. bottles. Betadine Aerosol in 3 oz. bottles.

Samples and literature upon request.

...YET VIRTUALLY NONIRRITATING TO SKIN AND MUCOSA

TAILBY-NASON COMPANY, INC.
DOVER, DELAWARE

A new highly effective

SHALE TAR

Metashal®

Solubilized Colorado Shale Tar, Stiefel

"especially impressive...in atopic dermatitis of all ages and stages"[4]

Compatible with all standard dermatologic drugs, such as hydrocortisone, salicylic acid, menthol and iodochlorhydroxyquin.

METASHAL, a Colorado shale tar that is different from conventional coal tars, has been found to be "especially impressive . . . in atopic dermatitis of all ages and stages."[4] Another investigator has reported that it "seems to be particularly effective in many cases of atopic dermatitis" in infants and children.[1]

Confirming previous studies,[2] a report of 414 cases of atopic and contact dermatitis and other skin diseases showed that shale tar therapy resulted in a favorable response in 96.3%.[3]

In another report of 365 cases from several different investigators, "excellent" or "very good" results were obtained with METASHAL in 93.75% of atopic dermatitis cases in infants and children, and fair to excellent results in 94.4% of atopic dermatitis cases in juveniles and adults.[4]

SUPPLY: METASHAL OINTMENT, containing 8.7% shale tar, for heavier, lichenified, subacute and chronic lesions. METASHAL LOTION, containing 18% shale tar in zinc oxide-talc shake lotion, for moist, more acute phases. Available only on your prescription.

SEND FOR SAMPLES.

REFERENCES: 1. Howell, C. M.: N. Carolina M.J. 18:322, 1957. 2. Brandt, R., and Dexter, H.: J. Invest. Dermat. 15:163, 1950. 3. Brandt, R., and Dexter, H.: Ibid. 19:409, 1952. 4. Brandt, R., and Szolomejer, W.: A.M.A. Arch. Dermat. 76:241, 1957.

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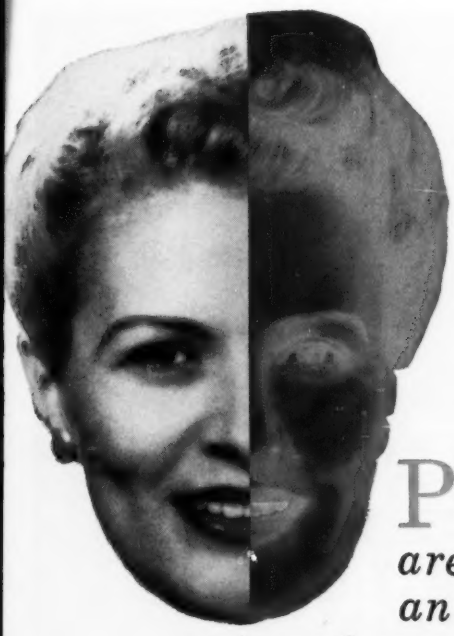

PSORIATICS

are half personalities, for an uncomfortable person is only one half a personality

EPIDOL®

will help to restore the psoriatics' appearance and self-confidence.

EPIDOL is a clear, *adhesive, non-greasy,* rapidly drying, improved Wright Liquor Carbonis Detergens plus Salicylic Acid 3%.

EASY to apply. Applicator comes with every bottle.

EASY to remove. Readily washes off with soap and water.

Discover how rapidly and effective EPIDOL may relieve the discomfort and clear the lesions. It helps restore the patient's feeling of comfort. Your psoriatic patients may, once again, become confident, full personalities.

SUPPLIED: Bottles with applicators: 3 fl. oz.—6 fl. oz.

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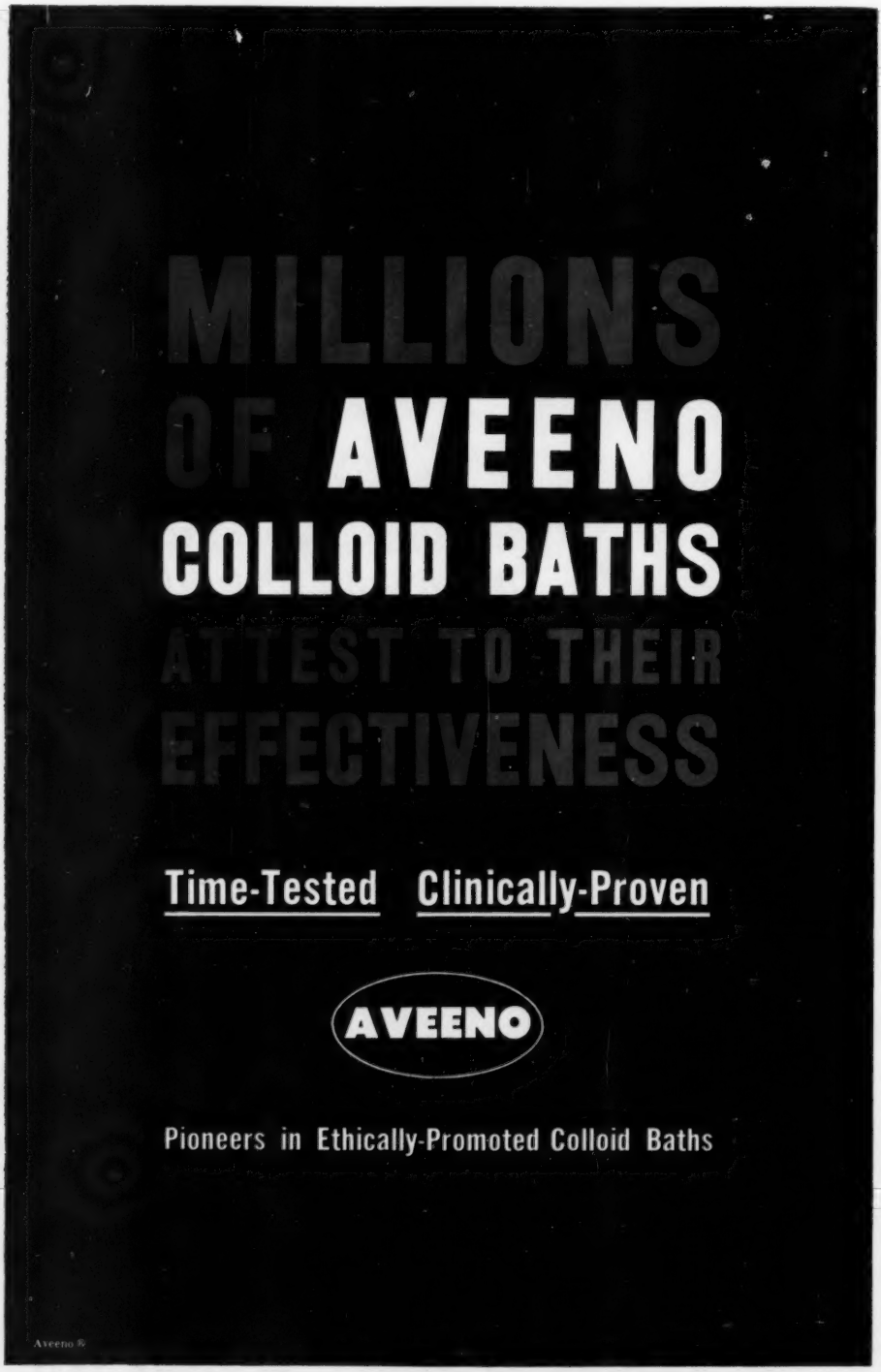
Samples, literature and reprints are available. Just write to:



Aveeno Colloidal Oatmeal is available in 18 oz. and 4 lb. boxes.

SOAP

AGGRAVATES...

PROLONGS

DERMATITIC CONDITIONS

Soap, because of its high alkalinity, can be a primary cause of skin irritation. Or it can aggravate a dermatitic condition already present...make it worse...and even prolong it. Lowila is soap free...does not contain alkali, fatty acids or perfumes. Lowila cleanses tender or dermatitic skin without irritation...maintains the normal acid mantle of the skin...creates an environment favorable to therapy and normal healing.

Lowila should replace your patients' regular bar soap for washing, bathing and shampooing. It easily works into a rich, gentle lather in both hard and soft water.

Soap irritation wastes sound dermatologic therapy . . . recommend Lowila Cake.

WESTWOOD *PHARMACEUTICALS* *WRITE FOR SAMPLES*

Division of Foster-Milburn Company, 468 Dewitt Street, Buffalo 13, New York

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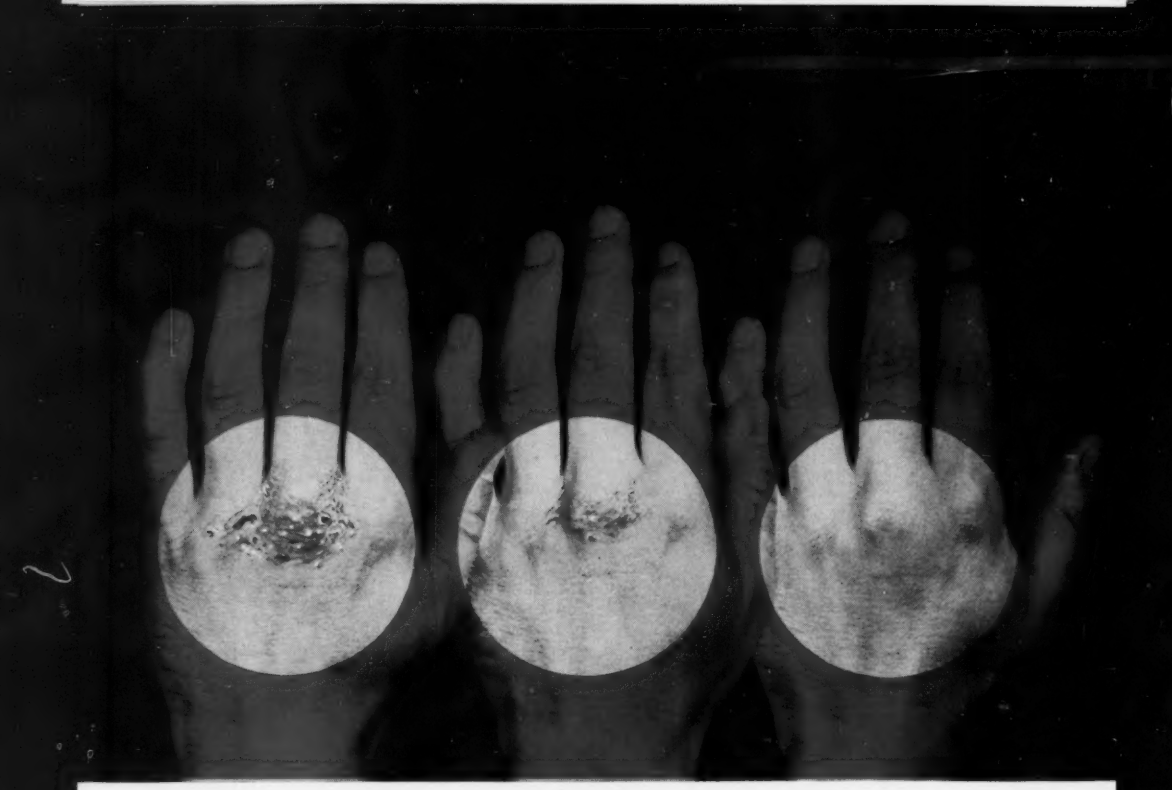

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A.M.A. ARCHIVES OF
DERMATOLOGY

Embryon Truths and Verities Yet in Their Chaos

A Discourse on the Unities of Medicine

WILLIAM B. BEAN, M.D., Iowa City

This address is of particular interest because in December, 1927, at Nashville, Dr. William B. Bean's father, the late R. Bennett Bean, an anthropologist and anatomist of some distinction, gave his address as vice president and chairman of Section H, Anthropology, at the American Association for the Advancement of Science. The title was "Stature Throughout the World." It is a happy circumstance that this particular line of family tradition is being carried on in such a distinguished way by this second generation of the Bean family.

P. S. R.

Introduction

Everyone in science has a latent or unrecognized yearning to add a small brick to the edifice of human understanding to enhance man's dignity and make more secure his fragile hold on nature. In this and other matters each of us strives to reach goals of his own choosing, using his own means and whatever skills he may have. Below the surface, unseen forces embedded in us from all our past experience are said to condition our conduct in mysterious ways. Since the goals most of us choose voluntarily are full of vanity and often are chosen unwisely, we may have the wrong objectives. But here fate steps in. We rarely reach our goals. So, if we have set our heart's desire on false ones, failure becomes fortunate.

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From the Department of Medicine of the College of Medicine and the University Hospitals of the State University of Iowa.

Chairman's address for the Section on Medical Sciences of the American Association for the Advancement of Science, delivered Dec. 28, 1957, in Indianapolis.

When I finished medical school I was certain that I wanted no part of academic medicine, but my teachers could not answer some of my simple questions. Sometimes I was amazed at what seemed to be their casual apathy. I had to do my own hunting. Now, years later, I can imagine no other career so worthy or so rewarding as one which combines caring for the sick, teaching, and research. Even the bane of administration is a small price to pay. Everyone must work for a living. Everyone should contribute to the welfare of the community and the welfare of mankind. He is a favorite of the gods who finds that his duty is a pleasure and that he gets rich intellectual and emotional satisfaction in doing what he must do and being paid for it.

I am mindful of the honor done me by my election to this office. I realize that I am expected to deliver an address with some bearing on science, medicine, and their place in our life today. I do not know how I came to be selected, but I am naturally elated. So far as I know no one ever turns down such an honor and obligation, though others must have shared my original impulse

to do so. To be honored by one's peers is a challenge which cannot be evaded. I shall talk to some extent of my own work and my special interests in the skin. To feign modesty and protest my inadequacies would be a sorry vote of confidence in those of you who got me into this fix. My task is to captivate my captive audience.

Clinical Versus Laboratory Research

Today the world of medicine and science is very powerful. It is the somewhat surprised recipient of almost too much faith from laymen everywhere. Thus, now more than ever it is urgent that those who transform ideas into action for the betterment of man, those charged with teaching future doctors, and those engaging in clinical research be sound and wise in their policy and practice. I shall look particularly at the relations clinical medicine, practical and investigative, has with the basic sciences, so called. I need not emphasize that my conclusions are provisional, as all interpretations should be. I am interested that with maturity I am losing a proprietary interest in my own opinions. I am uneasy when others try to force them to harden into dogma. Our equity in ideas should be in their continual refreshment and not in their eternal verity, for truth changes as new light alters or obliterates old shadows and silhouettes. Science is ill served by squabbles over priority and intellectual squatters' rights.

In our day no individual man is able to cope with the bewildering complexities in which he is enmeshed. Especially is this true of science and medicine. We have tried in two ways to escape to a tenable position to survey the terrain. These are by the specialization of knowledge and by the erection of institutions. Indeed, institutions themselves foster specialization by division of labor. Thus trying to solve complexity we have achieved isolation. The corpus of knowledge keeps breaking into ever small subdivisions tended by workers not only inarticulate in other fields but largely unaware of them. Analysis, the partition of knowledge and its advance on a multitude of separate fronts has not seen the complementary development of synthesis, the weaving of what often seems to be a tangle of old and odd threads into a new cloth with a fresh pattern.

Dermatology

In talking about the sciences, basic science and its sometimes belittled mother, clinical science, my excursions into the realm staked out by dermatologists give me ample reason to seek out certain muted chords, variations on the theme of *the unities of medicine*. And this is appropriate, since our theme at this meeting is the skin—a covering common to all and a fitting topic for discussion.

The specialty of dermatology, not yet a hundred years old, arose when man really began to look at himself and then think about what he saw. Its pioneers explored and catalogued. They mapped unknown land. As biologists they were natural historians of disease. Being educated in the classics, they erected a formidable list of Latin and Greek names for warts, pimples, poxes, and rashes. At times the practitioners of the art of dermatology were guilty all unwittingly of that ancient abdication from reason, the heresy that to name was to know. Physicians always must be alert to keep in mind the fact that giving a name or making a diagnosis is the beginning and not the end of wisdom or even of learning. The act of naming a disease has never quite escaped from the ancient priest-physician's belief that naming gave control. Thus, before dermatology was fairly launched as a special interest in medicine, it was nearly sunk by a naive faith in nosology and a system of nomenclature, sound in principle but holding the danger that it become deified in a static iconography not recognized as ultimately false in that it was fixed. My former chief, the late Dr. Blankenhorn, a superb clinical teacher, used to say that he shared the dermatologists confusion but not their terminology, a statement fortunately

no longer justifiable since dermatology has emerged as a clinical science.

The next move was the unhappy separation of dermatology into a specialty apart from general medicine. This looks innocent enough. At first it is, because individual specialists were physicians whose talent or taste led them into a particluar field—in this case, dermatology. But as a clinical specialty grows it wants status. It needs status. Its devotees band together. They form societies, publish journals, and quarry out a block of time in the curriculum of medical schools. At length a hierarchy of elite members determines who shall be allowed to call himself a dermatologist. It *pre*scribes certain final conditions of study and experience, *pro*scribes others and admiringly sets a halo on its own head. Eventually a self-perpetuating board of censors, beholden to no medical college, without charter as university, determines rigid requirements for study, qualifications for admissions to the examinations, and repeatedly fluctuating rules for certification. Thus the heavy hand of the stereotype is raised to stifle originality.

The loss to general medicine is to forget to study the skin. This loss is great or only moderate, depending on whether departmentalization in teaching, research, and practice separates not only individual persons but the free interchange of ideas. The loss to dermatology is the tendency to see medicine as skin deep or not even skin deep but as an isolated problem, a bit of churning flotsam to take to the laboratory rather than part of the bewildering complexity of man. In disease and health man cannot be understood piecemeal, even if he has to be studied that way.

But the wisest practitioners of dermatology and medicine have never lost sight of the essential connection of the two in the larger unity of general medicine. The danger has been rather that those who have narrowed their focus to a particular aspect of structure, function, or disease of the skin will lose perspective or that those in basic science have something of importance for clinical medicine but knowing little medicine fail to establish contact. Basic science is essential, for we cannot expect to advance learning without using to the full skills existing only in the laboratory. Indeed, help often comes unexpectedly from work along very different lines from those we are pursuing.

Complexity—the Plight and a Solution

Physicians who are teachers have known for some time that neither all the facts nor all the skills can be learned by undergraduate students, not even in the long later years of apprenticeship to qualify as specialist. We have not resolved the problem that while *ultra*specialization is essential in most research, it is bad for teaching, deadening to the practice of medicine, and may even be fatal to the patient. Solution may be impossible. But we cherish hope that man will not be lost in a sea of confusion, utterly overwhelmed by the great surfeit of undigested facts, shipwrecked by an overweight of knowledge.

Two methods have been suggested to find a way out of our increasing confusion in practical medicine. At one extreme is the plan to emphasize laboratory research further and separate it from practice and teaching. The medical school of the future is seen as a cluster of research institutes to which the hospital-clinic is attached as a necessary but scarcely honored appendage. Or a great hospital is built expressly to study disease, not to heal the sick. Clinical medicine becomes a parasite on basic research. At the other extreme, we have individual clinical teachers and practitioners who personally have had training in chemistry, physiology, physics, or other fields and who do with their own hands the researches suggested by the puzzling troubles of sick patients. Too often they are old before their training is completed and they can get on with their work. Nevertheless, this seems the best though the most costly solution. Midway between, we have Ph.D.'s with a home base in a clinical department.

They are uneasy about losing identity with their primary group. They may have joint appointments in biochemistry and medicine or dermatology. Or collaborative effort goes forward as a true partnership. Too often the clinician may seem to, or actually try to, exploit someone in basic science to do his work for him. No form of research which employs slave labor can flourish. Slave and master alike decay. But those in basic science must recognize the essential role of clinical research as well as its profound difficulty and vexing frustrations. Lacking the neat precision of the laboratory, it shares the same rigorous disciplines, scepticism, and critique.

Poor contact between basic science and clinical medicine is illustrated in the long lag from the early clinical knowledge of antiscorbutic foods, and of the circumstances under which scurvy appeared, to the final isolation and synthesis of ascorbic acid. Just over 200 years ago, James Lind summarized his extensive medical experiences in the British Navy in his treatise entitled "The Scurvy." He defined the disease, expounded its cause, described its cure, and illustrated its prevention. As an example of the ponderous movement of bureaucracy the Lords of the British Admiralty adopted Lind's recommendations as official doctrine for the Royal Navy at about the time of his death, after a lapse of only 40 years. But an even more ponderous delay occurred in the 125 *more* years which were needed before students of chemistry and physiology finally got around to the isolation and synthesis of ascorbic acid. During the last two decades, many in vitro functions of ascorbic acid have been clarified but not the mechanism of its function in man.

Another delay in understanding medical problems, worked out from the solitary point of view of a single laboratory specialty, is illustrated by the fact that the clinical diagnosis and understanding of myocardial infarction, ancient history to the pathologist, was not made until fairly recent times. To be sure, the electrocardiograph was very helpful, but it could not be applied until clinicians, led by Herrick, Dock, and others, recognized that infarction of the heart was not invariably fatal. Many more examples could be adduced to suggest at least a partly negative answer to Trotter's searching question, "Has the intellect a function?"

Thus, the past saw much reluctance of those in basic science to tackle the problems of clinical medicine. Under the impact of laboratory research, change began. It has continued with accelerated speed. The trend of neglect has been reversed completely in a few spots. Laboratory scientists have outstripped the clinician in knowledge of certain biochemical problems relating to nutrition. We are in the uneasy situation of having vitamins whose function in man is not known and must be inferred by extrapolation from known or suspected biological functions in lower animals and from in vitro studies.

Let us then consider some of the differences between laboratory and clinical research, recognizing that no fixed line separates them. There *are* real differences. Among the paradoxes which may confound an easy understanding of the relations of laboratory science and clinical science is the problem of normality, individuality, and the textbook picture of some specific disease. The more closely science in the laboratory approaches complete mathematical specification, the further molecular and physical systems must be abstracted from the actuality of their infinitely more complex relationships in a living man. Thus, as science becomes more exact it tends to lose contact with medical reality, or at least it runs that risk. One cannot escape the view that laboratory science is not always on guard lest, impelled by techniques and constrained by apparatus, it give an ironic answer to John Hunter's impetuous questions: "Why think? Why not try the experiment?"

Whereas clinical science may be depreciated because of its inherent vagueness and complexity, laboratory science as it explores

deeper and deeper takes on a cast of unreality which always skirts the haunting possibility that it is beguiling itself by reproducible artifacts. If we refuse to grant significance to anything which cannot be proved in a laboratory, we have gone a long way toward convincing ourselves of the truth of the ancient charge against Socrates that he was trying to prove that the lesser is the greater thing.

The Kinds of Clinical Science

The study of patients with lesions of the skin may be approached as descriptive natural history. Knowledge of natural history enables us to identify a disease or lesion, to infer its cause, to predict its probable course, and to forecast the outcome. Experience and what can be taught of others' experience enable us to identify and then study the phenomena of disease, their probable interrelationships, and the consequences. Disease may be defined as the reaction of the body to some injurious force or forces which may not always be known. From the train of events observed in a series of persons sick in the same way, we generalize what is called a textbook picture, a useful figment but still a figment, since no patient will have all his signs or symptoms at the dead center of an average and keep them there. We must recognize disease in this way to estimate severity, to judge prognosis, and to evaluate treatment. No matter how clumsy this tool may be, it is the only one we have in clinical medicine. If we scorn it for the cleaner-cutting edges of speculation and arbitrary systems we mix weed and wheat in neat but unusable bundles.

The other major form of clinical research is mechanistic in intent and mechanical in procedure. It has as its function the study of how things work. Bleeding, pain, itching, and imbalances in the acid-base metabolism are its subject material and only incidentally the study of disease and perforce but sometimes reluctantly of the sick man. Its method is experiment; its guide, technique, its means, an instrument. It has many notable exponents and was brought into a noble state of fruition by such people as Mackenzie and Thomas Lewis in England and Soma Weiss in this country. Its contributions are far too numerous to mention. Much of this symposium on skin disease exemplifies it. Its danger is that it becomes too selective, views with oil immersion before scouting with lower powers, and, if not eternally vigilant, does research on such a small fraction of the phenomenon that it shares the danger of other laboratory research by becoming an abstraction and losing reality.

There are different kinds of clinical observation. I shall illustrate some of them. Clinical observation depends on training, on active curiosity, and on the ability to see the importance of the unexpected or to recognize the unusual when one is diligently searching out the usual, the commonplace, or the anticipated phenomena of an experiment. In fact, the ability to distinguish a new phenomenon or to recognize certain obvious aspects of reality is so rare that it takes on some of the quality of creative genius.

Looked at from another point of view, clinical research finds room for employment of at least three kinds of activity which have no necessary rank order of excellence. The most primitive type of observation is that which everyone practices every day. By it we identify objects we see. We are enabled to thread our way through the maze of traffic on a busy street, preferably with the help of traffic lights and traffic policemen. It helps us identify the bark of our dog at night and to know by sound of voice or step members of our family and close associates. Carried slightly further along, it is the method by which practitioners a hundred years ago and, of course, today diagnose and prognosticate. It sees the splinter hemorrhage and the small purpuric lesion at a time when more casual observation or an untrained person would miss them. It knows when to mistrust a laboratory report as obviously in error or probably

wrong. As it is applied to the art of medicine it is called clinical hunch, or intuition, because it depends on economy of effort which takes many mental steps unconsciously to arrive quickly at the proper destination over unseen stepping stones. Though it may be looked upon by the novice as almost magical, there is nothing magical about it. It is simply the sifting of essential from spurious which occurs so rapidly that conscious intellectual effort cannot be seen to have been part of it. A skilled physician thus practicing may not be able to explain the devious paths he took and how he seized on the cardinal features almost in an instant.

This kind of observation is hardly research. It takes the experience of the person and blends it with what he has learned from others. It is not likely to find new discoveries, either. It is impossible to communicate in its entirety and must be built up by each physician for himself, but clinical practice without it is null and void, despite laboratory brilliance and technical virtuosity.

A second type of clinical observation comes close to approaching the highest creative intellectual activity, in which imagination fashions art or discovery. Pasteur had the imaginative and intuitive approach. Some new and luminous truth apparently arises spontaneously but usually after intensive thought and frequently after deep meditation, or it may come from no apparent stimulus or obvious connection with any conscious mental activity. As examples, one can cite Fleming's realization of the possible significance of the troublesome inhibition by the growth of a mold of his special bacterial friends, the luminous ideas which inspired Castle's work on the pathogenesis of pernicious anemia, Hench's observations of pregnancy and liver disease as unexpected relievers of the symptoms of rheumatoid arthritis, and Gregg's recognition of the association between German measles early in pregnancy and the occurrence in the offspring of congenital deformities. As Spence said:

> This kind of clinical observation for which I can find no suitable name is one of the most scintillating starting points of scientific research, but we cannot order it or command it. The best we can do is to recognize its possibility in the sensitive few, and to prevent its inhibition by too much teaching, its submersion by too much dogma, and its extinction by too much ritual even though it might be the ritual of research.

The third form of clinical observation is perhaps more clearly recognized as Lewis' clinical science or our clinical research and clinical investigation. It requires, first of all, (1) an idea based on (2) observation. This idea brings to mind (3) a question. The question must be formulated precisely with these things in mind: (4) that it is worth asking, (5) that it has not already been answered by someone else, and (6) that in the precise form in which it is asked it will provide an answer which says yes, no, or how much. Then, and this is often overlooked, (7) it must be asked by someone who has the qualities of intellect and endurance to do the actual work necessary to get an answer and, finally, the answer must be able to be (8) perceived, (9) understood, and (10) communicated, not necessarily in deathless prose but in something besides a series of tables and charts. Its purpose is to get new knowledge or to make more sense out of old knowledge by a new alignment of facts already known.

The capacity to reach excellence in these forms of observation depends on several qualities: First of all, curiosity. Each must retain some of the boundless excitement, the glow of wonder, and the incorrigible persistence of the child as he begins to find his way around in a new world. Unfortunately, this curiosity may be stifled by our system of education, with its great emphasis on memorizing masses of details. The next qualification is skepticism, which leads to a critical view of all the phases of observation, experimentation, interpretation, and the drawing of conclusions, and a third qualification includes some of the elements of a prophet, which at its highest approaches

the wisdom of Galileo, who believed that phenomena could be ordered into "natural law gradually attainable half by discovery and half by creation."

Vascular Spiders

I shall talk briefly about vascular spiders and other vascular lesions of the skin. When I was an intern at Johns Hopkins, spiders with liver disease were accepted but no one could tell me why. At Harvard I could get no help from Minot, Castle, Weiss, and other great men of the Thorndike. In Cincinnati, Blankenhorn encouraged Donald Forster, Morton Hamburger, and me to go on with our study. Cirrhosis was plentiful. I saw dozens of patients with spiders. Serious doctors thought this a quaint but harmless passion. Before long I was called to see some of the residents' wives, who got spiders while pregnant, had no liver disease, and lost the spiders after pregnancy. After reading Walsh and Becker's paper on spiders and palmar erythema, I found that I had been seeing and writing notes about curiously red hands without registering anything. At length I had collected systematic notes on 250 persons with spiders, searched for reports buried here and there in medical writings, and meditated upon the strange association of spiders and palmar erythema with chronic liver disease and with normal pregnancy. Medicine had become so specialized that no one else had been aware of the eruption of spiders in both advancing liver disease and advancing pregnancy. I suggested that estrogenic hormones, natural in pregnancy, accumulating in excess in disease of the liver might cause this change in the blood vessels of the skin as well as produce the long-known effect on endometrial and myometrial spiral arteries. Giving estrogens to a few subjects encouraged me to believe that the idea was valid.

A time for reflection, speculation, writing, and rewriting came with a four-year turn in the Army, when I was detached from clinical work. A monograph was produced which I thought would sink into the vast ocean of medical literature without a splash. The effect was pleasantly different. Hepatitis, not the confidently expected influenza, was the epidemic of World War II. Despite my detailed description of the arterial spider, and hereditary hemorrhagic telangiectasia, mistakes are made repeatedly. Many useful signs are missed. Others are misconstrued. Since the patient cannot be examined by a laboratory, errors may arise from lack of effort and of knowledge. In recent years I have described in detail many of the hitherto uncodified features of a variety of related lesions. I will take you for a brief tour through my gallery.

Here the main clinical features, the significance, and some aspects of pathogenesis of several vascular lesions of the skin were illustrated by slides and movies. The detailed studies upon which this discussion rested have been reported in a series of papers and mongraphs listed in the references, where may be found a discussion of the writings and ideas of other investigators too.[1-16]

The Discipline of Method

I have evolved a plan for the systematic collection of data on vascular lesions of the skin. It seems so simple as to be scarcely worth bothering you with, but such a systematic study is too much trouble or too drab for most physicians, dermatologists, or internists. Somewhat surprisingly, I have become an exponent of what used to be called, with grace and feeling, natural philosophy. I have found it convenient to collect and record information along these lines:

1. Decide what kind of a lesion is to be observed and evolve a careful description and definition of it. I now keep notes on several dozen vascular lesions and related marks in my patients.
2. Determine and record the topography related to the microcosmic geophysical anatomy of skin and mucous membrane.
3. Is there a relationship to sex?
4. Is there a relationship to age?

5. Is there a connection with disease or other states, such as pregnancy, or is it a parameter of health?

6. Do such factors as race, complexion, skin color, or occupation have any bearing on the problem?

7. Are there temporal factors of clock or calendar related to onset, growth, course, ultimate fate, changes, and circumstances of coming or going of a lesion?

8. Analyze the gross and microscopic morphology of the lesion.

9. Evaluate geographical and environmental factors.

10. Historical aspects may be left conveniently for later, lest prejudice or established error influence one too much. Since most lesions will be known already, we are not really beginning from virginal ignorance.

11. Employ the methods of chemistry, physiology, and any other appropriate science to explore leads which are uncovered in the clinical study. This may be the work of a few weeks or a lifetime.

12. Go back to patients and verify the products of laboratory research.

13. Communicate useful findings and employ them in practice and teaching.

14. If possible integrate the whole and synthesize the knowledge into practical wisdom and erect hypotheses, not as a corral to keep unbroken horses in permanent stockade but as a scaffolding to be taken down when a particular part of the structure of science is built solid.

As I have continued to expand my observations, I have become aware of two things. One is the profound difficulty of seeing perceptively what is there. Loss of intellectual energy is the price we pay for strict and complete concentration. We live in a day of distraction, when only the very persistent or the truly great can sacrifice that part of themselves which is used up with complete attention. The process resembles on a small scale what happens to a bee when it stings. It is too painful for most of us to try.

The second may be part of the humility arising from experience. Fortunately it comes often to those whose life is spent in teaching and practicing medicine. Progress is too fast for us. Medicine has made truly splendid advances. These are being spread before you at this annual meeting in impressive splendor. We expect such excellence to be so routine that we hardly praise outstanding work. But those of us who daily confront patients who have troubles large or small, banal or fatal—how little do we know of the minute temporal anatomy of disease and its causes, ecology, and precise unfolding in John Smith, a single unique person, who is changing before our eyes as he is influenced by all the myriad variables of seed, soil, fertilizer, and climate. How rare it is for a physician, resident, or undergraduate student to trace entirely through even one night watch the kaleidoscopic movements of all the little secrets of a sick man and his disease. And how much rarer is such a vigil, measured in months, years, or a lifetime, as a patient shifts from work, to home, to doctor's office, to hospital, out again, and to the cure or fatal end of his disease. We know that the textbook picture, at best a matter of averages, never suits a given patient in all particulars or for long. How rarely can we pinpoint the secular trends with precision or generalize clearly data collected by diligence. How few of us are aware of all the turbulent variables as we pursue our clues amidst a network of shifting, bending, and seemingly elastic coordinates. This is no idle demonstration at the wailing wall, and I hope my plea for excellence and work demands no more than we can evoke of diligence taught by discipline to become clinical wisdom. If we cannot realize these objectives, we might as well mechanize medicine and put it in the hands of engineers and bureaucrats, who suspect that they can make it more efficient and pretty it up by automation. No. Everyone in clinical practice, if he has any compassion and any perception, knows that too often he is at the mercy of uncertainty. And this lack of certainty is born of ignorance about the knowable. It is the failure to observe rather than the inaccessability of facts. It cannot come from laboratory research, and without it the spectacular know-how of the laboratory may lead to nothing more than abstractions—*bombinans in vacuo*. My thesis is that we will never improve the situation

unless we can attract into the arena of the sick dedicated workers who will observe attentively, collect data, and trace to their best capacity things obviously important and obviously unimportant. Until the small shoals as well as the giant headlands of disease have been mapped, we shall move with the halt, the lame, and the blind in our recurrent shipwrecks.

Conclusion

Well, as happens on any journey into a new land, I started out confidently enough in familiar territory and made good progress for a time. Soon the trail faded out. I stumbled on. Perhaps I was not even as sure of where I was as Daniel Boone, who, when asked late in life if he had ever been lost in the wilderness, pondered a bit and answered, "No, but once I was bewildered for three days." With overmuch effort I have arrived at some simple platitudes, axioms, I believe, for anyone concerned with mankind as a biological phenomenon, and something more—men and women—the persons he knows and the patients he studies and treats.

I maintain that science and medicine cannot achieve their best purpose until clinical science regains its status as the mother of sciences. This is not to be done at the expense of laboratory research or even in competition with it. Clinical and laboratory science must be partners of equal stature. Collaborative research, a team of horses yoked together, may not win any Derbies but might win some chariot races. If we continue emphasis on projects, piece work, equipment, and techniques at the expense of clinical work, medicine will suffer. Laboratory work must not be directed by machines, reducing each problem to an artificial fiction with only one variable, for then it is separated so far from reality that its numbers are mere abstractions. Clinical medicine must concentrate on the particular, watching many things at once, frustrated by variables out of control and many not even known, limited by what it may do in manipulative experiment but alert to make the most of Nature's experiments which no laboratory can duplicate. It must guard against diffuseness, premature generalization, and the conception of biological truth as fixed. For it is only by warm cooperation of men in the various special disciplines, such as chemistry, physiology, physics, and pathology, with clinicians that greater biology will lead to a better understanding of man. I trust that at least the theme of my discourse is in keeping with Sir Thomas Browne's wonderful words of old from Christian Morals, "Let thy studies be free as thy thoughts and contemplations: but fly not only upon the wings of imagination; join sense into reason, and experiment unto speculation, and so give life unto embryon truths, and verities yet in their chaos."

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Histogenesis of Basal-Cell Carcinoma

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Introduction

Basal-cell carcinoma has interested scores of investigators because it is seemingly a biologic enigma. It appears that a tumor derived supposedly from the more primitive epidermal basal cell is biologically less active or malignant than a tumor derived from the maturer "child" of the basal germinative cell, the prickle cell. This situation appears unique in the skin: Tumors of squamous epithelial mucous membranes, such as the cervix of the uterus, gingiva, buccal mucosa, esophagus, and the like, also apparently of basal-cell origin, follow the rules, and are more malignant than tumors presumably of the maturer prickle cell.

The purpose of this report is to clarify and enlarge upon our previously expressed attitude (Smith and Swerdlow), namely, that basal-cell tumors arise from hair anlage. It is my feeling now and the thesis of this report that basal-cell carcinoma is less malignant than prickle-cell carcinoma because it represents an abortive attempt at the formation of hair follicles, a mature and differentiated structure with at times admixtures, albeit rarely in our experience, of adnexa that develop embryologically with the hair follicle, the sebaceous gland, and, still more infrequently, the apocrine glands. These ideas are not new, and these views come very close to those of Adamson, Mallory, Haythorn, Foot, Lever, and Pinkus (1953). It should be here mentioned that this is still a minority opinion.

Our previous work is reviewed, and additional tangential evidence is presented in support of the "hair anlage" concept. The evidence is from a study of the epithelial and stromal components of basal-cell carcinoma and trichoepithelioma and a comparative consideration of basal-cell tumors with the embryogenesis and histogenesis of hair—development, growth, replacement, and regeneration.

Submitted for publication April 17, 1958.

Materials and Methods

This report is of a continuing study over the past four and one-half years of 291 basal-cell carcinomas from 260 patients. All of these tumors were stained with hematoxylin and eosin, toludine blue in citric acid buffered to pH 5, and periodic acid-Schiff reagent. Appropriate controls were similarly stained. Additionally, sections of skin from various body regions obtained surgically and at necropsy were similarly stained, as were sections of skin from all body regions of embryos and fetuses ranging in size from 1.0 cm. to full term. Tissues and lesions examined were as follows: normal adult skin, normal child's skin, normal fetal skin, basal-cell carcinoma (291 lesions), trichoepithelioma (10 lesions), seborrheic keratosis (100 lesions), senile keratosis (10 lesions), squamous-cell carcinoma (10 lesions), sclerosing hemangioma (10 lesions), and miscellaneous lesions (169 lesions). Particular emphasis in this study was given to the hair follicle and adnexa. Most of the tissues were fixed in isotonic neutral formalin; some few specimens, in Zenker's, and some, in Helly's fluid.

Comments on Literature

Basal-cell carcinoma was first described by Jacob (Jacobean ulcer), in 1827. It was, however, Krompecher who in 1900 and then again in 1903 first thoroughly described these tumors and named them basal-cell carcinoma. He ascribed the origin of this tumor to the basal cells of the rete Malpighi. In 1903 he applied the diagnosis to all noncornifying squamous-cell carcinomas of the mucous membranes, including gums, cheeks, pharynx, nasal mucosa, larynx, esophagus, vagina, bladder, cervix uteri, salivary gland ducts, and prostate and even to melanomas. It is of interest that the opinion of Krompecher is dominant today (see Willis, Teloh

and Wheelock, Montgomery, Ewing, Allen, and others). It is also of interest, however, that Krompecher considered possible an origin from hair follicles and sebaceous and sweat glands.

Allen feels that basal-cell tumors arise from basal cells of the epidermis and/or hair follicles and cautions that the presence in these tumors of cells similar to those which line the epidermis and hair follicles, although evidence for origin from these structures, is not equivalent to maintaining that the hair matrix in one or another phase of its development is the source of basal-cell carcinoma through dysontogenesis. Allen does recognize a tumor of hair follicle origin, the so-called trichoepithelioma, Brooke's tumor, or epithelioma adenoides cysticum.

Pinkus (1953) feels that basal-cell tumors arise from pluripotential cells present during postnatal or adult life which can differentiate in the direction of sebaceous, apocrine, or hair structures. Pinkus points out, as others have and as seems to be the case, that the various derivatives of mammalian ectoderm retain quasiembryonic potentialities into adult life. The emancipation of these adult but "pluripotenial" cells leads to their transformation into tumor cells at the time the epithelioma actually begins to grow. The views of Pinkus come close to those of Lever, who believes that basal-cell tumors are derived from the primary epithelial germ. Pinkus points out that the primary epithelial germ, if it did persist into adult life and especially if it were reduced to its simplest imaginable form of one cell, would not be any different from, but would be synonomous with, "pluripotential" cell or cells. The primary epithelial germ, he maintains, is a transient structure which almost immediately becomes differentiated into the adnexa derived from it. The Fox brothers (in Dubreuilh and Auché) were the first to propose a derivation of the rodent ulcer from the hair follicle. Verneuil (in Pinkus, 1953) favored a sweat-gland origin; Borrman, a derivation from aberrant epithelial germs separated from the epidermis during closure of the facial clefts or during genesis of the adnexa; Glasinow and McFarland et al. (in Teloh and Wheelock), a relationship to the embryonic facial clefts, and they called them "facial cleft carcinoids" derived from developmentally sequestered cells.

Eichenlaub and Osbourn, in an attempt to explain the enigma of a less malignant tumor arising from an apparently more primitive germinative cell in the skin, tentatively concluded from a study of mitoses in pig skin that there was evidence to support the contention that the basal layer was not the germinative layer of the epidermis, that the germinative layer very likely was the lowest layer of prickle cells, and that it was the prickle cells that were concerned with proliferation. They felt that if the prickle cell was the primary germinative or functional cell of the epidermis this would explain the seeming biologic enigma of the greater malignancy of prickle-cell carcinoma and less malignancy of basal-cell carcinoma. Pinkus, on the other hand (1951 and 1952), showed in human skin, stimulated to rapid proliferation by stripping away the horny layer with cellophane tape, that mitoses occur in both basal and prickle cells. Pinkus also demonstrated, with tissue culture techniques, that the basal layer survives and forms new prickle cells and keratin. Toolan demonstrated a similar situation with human skin transplanted into previously irradiated rats.

Kyrle pointed out that the epidermis has two different functions to fulfill and therefore possesses two different potentialities for differentiation: One is its function to form surface epithelium and keratin, and the other is its function as a matrix for the postnatal formation of the adnexa. The resultant tumor of these cells, it would seem, depends upon which "epidermis" furnished the tumor cells, or otherwise the type of tumor would depend upon which of several potentialities of the epidermal cell was activated, basal-cell tumors forming when the adnexal potentiality was activated.

Adamson thought that basal-cell tumors were nevoid tumors originating from latent embryonic foci aroused from their dormant state at a later period of life and that these foci were embryonic pilosebaceous follicles and occasionally embryonic sweat ducts. He felt that it was not possible to sharply differentiate trichoepithelioma from basal-cell carcinoma and felt this to be the case because both had a common origin. Adamson felt that both were abortive attempts at forming pilosebaceous follicles, except that in basal-cell carcinoma the cells were embryonal.

Mallory thought that these tumors were of hair matrix origin. His feelings were based on the findings of fine longitudinal fibrils in the tumor cells which were identical in appearance to similar fibrils in cells of embryonal hair follicles and unlike the intracellular fibrils of epidermal prickle cells. Mallory believed that epidermal basal cells were early forms of prickle cells.

Teloh and Wheelock sought to corroborate the older concepts of Krompecher that these are tumors of basal cells as such—basal cells of the epidermis, sheaths of the hair follicles, and sebaceous glands. Montgomery's view is in general agreement. He feels that these tumors derive from basal cells of the epidermis, outer hair sheath, and sebaceous and sweat glands. Willis feels that basal-cell tumors have a multicentric origin and can arise from basal cells of the epidermis, pilosebaceous apparatus, and sweat glands, either singly or in combination.

Lattes and Kessler are of the opinion that the varied microscopic patterns of basal-cell tumors are strongly suggestive of an origin from cells having the same potentialities as those giving rise to the accessory skin structures. Although intracellular bridges are not usually seen in basal-cell tumors, some tumors, they point out, on occasion do have distinctly detectable intracytoplasmic fibrils which are the same as those described by Mallory. These fibrils were studied in a large group of tumors by Lattes and Kay (see Lattes and Kessler), and it is apparently their preliminary opinion that these fibrils at times resemble the myoepithelial structures of sweat glands while in other instances they are very similar to the fibrils in the cells of the outer layer of the hair follicle. According to them, the keratinization at times evident in basal-cell carcinoma does not resemble that which occurs in epidermis or in the well-differentiated squamous-cell carcinoma, mainly because there is no evolution through a prickle-cell phase. They feel that this process of focal keratinization rather resembles that of the hair follicle apparatus, thus strengthening the theory of origin of these neoplasms from specialized cells.

Wallace and Halpert feel that the cellular structure and behavior of these growths are such that they suggest that they do not arise from basal cells directly but from cells already differentiated to form hair follicles. They, like Pinkus, Hueck, and others, called attention to the epithelial-stromal relationship so evident in the peripheral palisading of the tumor cells and in the loose, fibrillar, newly formed stroma. Wallace and Halpert feel that these tumors arise from cells of matrix differentiated to form hair follicles or from hair follicle anlage that did not fully develop. The variation in histologic pattern, they believe, is dependent upon the degree to which the tumor growth imitates the structure of the hair follicle; they suggest the name "trichoma" for these lesions.

Haythorn subscribed to Mallory's view that these tumors were of hair matrix origin.

Welton et al. felt that many of the basal-cell tumors examined by them showed evidence of varying degrees of differentiation, simulating more or less abortive hair follicles and sebaceous and sweat glands, and that central whorling and keratinization in the nests of tumor were common, particularly if one included all cases with isolated or incompletely developed foci of central lamination and formation of squamous-like cells.

Mac Cardle, in a presentation recently at the International Academy of Pathology, expressed the view that basal-cell tumors take origin from basal cells as such; that Herxheimer fibers are visible in these tumors; that these tumors have intercellular bridges, as do basal cells, and that the mineral-ash content also supports a basal-cell origin. I feel that these findings, although consistent with an origin from basal cells, do not reflect the biologic potentiality of the basal cell, i. e., do not separate the epidermis-forming basal cell from the "pilogenic" basal cell.

Lever (see above) feels that basal-cell tumors originate from incompletely differentiated embryonal cells rather than from dedifferentiated anaplastic cells and that basal tumors are nevoid hamartomas derived from arrested embryonal primary epithelial germ cells and represent the least-differentiated group of primary epithelial germ tumors, the primary epithelial germ being a group of cells developed from the embryonal stratum germinativum from which develop the hair and the sebaceous and apocrine glands. It is Lever's contention that the variation in degree and direction of differentiation in the primary epithelial germ before the onset of neoplasia adequately explains the wide variety of histologic patterns of basal-cell carcinoma.

Foot feels that basal-cell tumors originate in distorted primordia of dermal adnexa rather than from ordinary basal cells, and he suggests the appellation "adnexal carcinoma" for these lesions. He states that these tumors imitate the embryonal development of hair and sebaceous and sweat glands, that there is a recapitulation of the genesis of the dermal adnexa in the majority of tumors, and that there is a distinct similarity in architecture of these growths and skin adnexa in their adult state. Basal epithelioma, he feels, is too general a term to be specifically descriptive, since there are more "dermatogenic" than "pilogenic" basal cells in the epidermis.

General Findings

In this continuous study, now of 291 basal-cell tumors, resemblances, some previously presented (Smith and Swerdlow), of basal-cell carcinoma to hair-follicle formation were evident (Figs. 1 to 5). We found the almost constant presence of small and larger foci of keratin material in the tumor nests. The pattern of keratinization was constant and striking and resembled that seen in the formation of hair. There were histologic examples of all types, no matter how classified. There was a whorled or laminated arrangement of tumor cells about keratotic or parakeratotic, central or eccentric, single or multiple foci. Exaggeration of this process produced outspoken horny cysts. The whorled cells in many fields were flattened and had elongated nuclei and generally were without prickles.

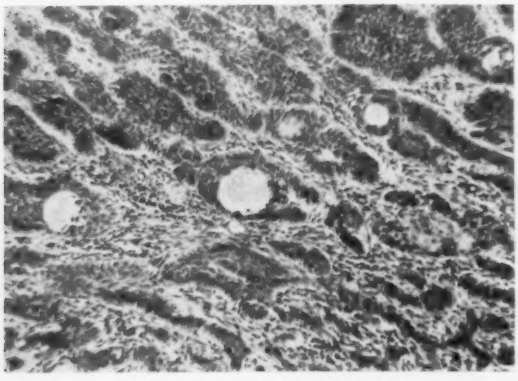


Fig. 1.—Basal-cell carcinoma, so-called pilar or keratotic variant, with numerous "keratin-whorl" foci and some outspoken horny cysts; × 100. (Reproduced from Smith, O. D., and Swerdlow, M. A.: A. M. A. ARCH. DERMAT. 74:286, 1956.)

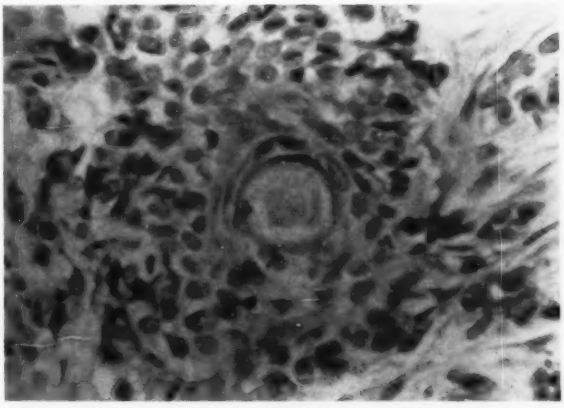


Fig. 2.—A nest of basal-cell carcinoma; abrupt central keratinization and lamination of surrounding basal cells; × 450.

The keratinization often was abrupt, as in hair follicles, and not gradual, as in squamous-cell carcinoma or normal epidermal maturation. There often were also nests of cells with palisaded, crowded, peripheral columnar cells and central haphazardly arranged cells that whorled finely and resembled either a late stage in the embryonic development of hair follicles or a cross section of an adult follicle at the level of the bulb where the inner sheaths are still persistent. The peripheral palisaded cells in places were vacuolated as are the cells of the outer sheath of the hair follicle; the centers of some nests resembled hair matrix cells. There were tumor nests that resembled all stages of hair development from embryonal germs to well-formed

Fig. 3.—Common variant of basal-cell carcinoma, showing epithelial-stromal relationship, peripheral palisading, fine central whorling, and circular, subtending newly formed stroma; × 100.

Figure 3

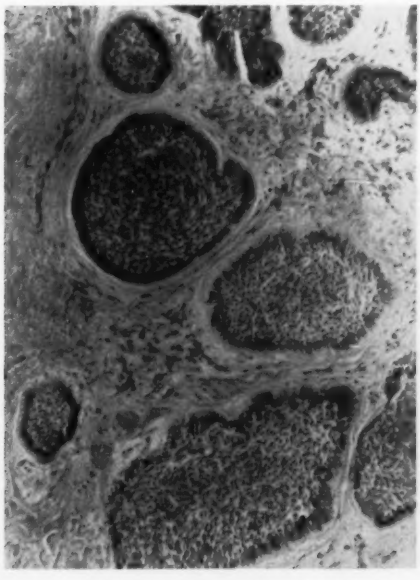
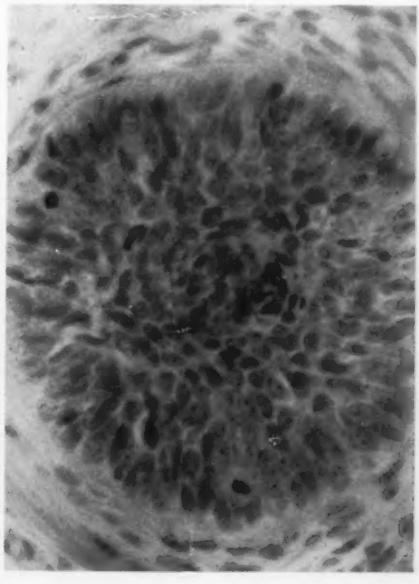


Fig. 4.—Higher magnification of Figure 3; × 450.

Figure 4



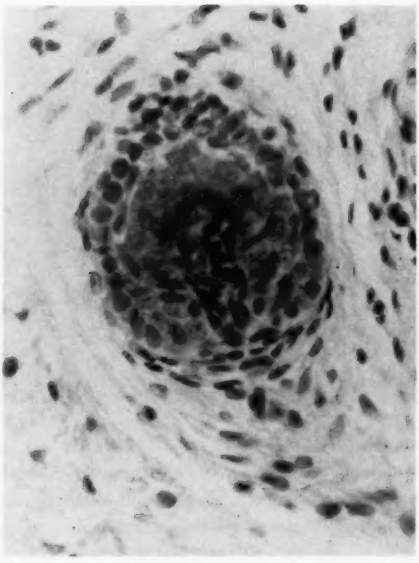


Fig. 5.—A nest of basal-cell carcinoma, with indented and altered subtending stroma; the resemblance here to a hair bulb or developing germ is great; × 100.

follicles as one went from field to field and lesion to lesion. The impression was that here was an attempt at hair formation, no matter how altered, abortive, disorderly, or neoplastic. The periodic acid-Schiff stain revealed in the majority of lesions a basement membrane or zone about the tumor nests not unlike that about hair follicles (Haythorn) (Fig. 6).

The horn cysts and foci of keratinization seen to a greater or less extent in almost all basal-cell carcinomas, particularly if multiple sections were cut, together at times with a pseudoepitheliomatous hyperplasia, often atypical, either of the overlying epidermis or at the edges of ulcerated lesions, resulted at times in the erroneous diagnosis of mixed or basal-squamous-cell carcinoma (Welton et al.).

Trichoepithelioma

Trichoepithelioma (Fig. 7) is the one "tumor" acknowledged by most observers, including those who subscribe to the view that basal-cell carcinoma takes origin from basal epidermal cells as such, to be of hair origin. We studied 10 typical and classical trichoepitheliomas and found in these tumors areas to me indistinguishable from basal-cell carcinoma. There were tumor nests with central keratin foci with or without abortive hair shafts and peripheral proliferated smaller crowded "basal" cells. We also found fields in most basal-cell carcinomas that were indistinguishable from "trichoepithelioma." There were some tumors that just defied definite categorization; in those instances, there seemed to be no sharp line of demarcation between the two. Clinical history then was resorted to, resulting in some interesting designations that ranged from "trichoepithelioma without keratinization" to

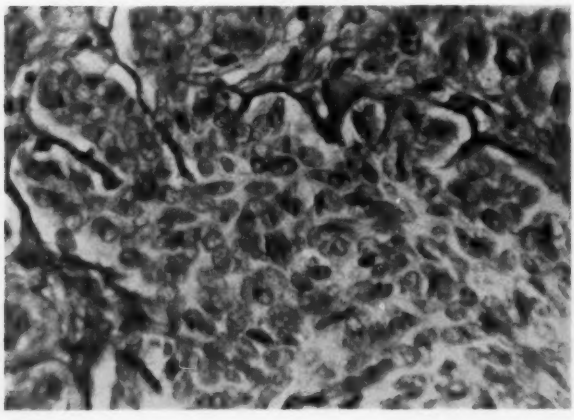


Fig. 6.—A periodic acid-Schiff-stained heavy "basement" membrane around masses of basal-cell carcinoma; × 450. Reproduced from Cervantes Ochoa, P.; Smith, O. D., and Swerdlow, M.: A. M. A. ARCH. DERMAT. 75:70, 1957.)

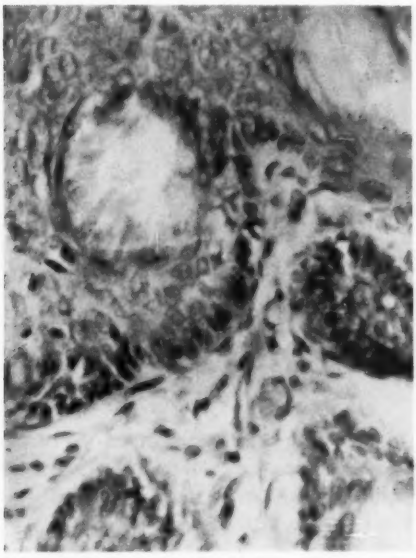


Fig. 7.—Nest of trichoepithelioma with abortive hair shaft and smaller nest resembling basal-cell carcinoma; × 450.

keratotic or pilar basal-cell carcinoma. Some few cases have, it is reported (Lever), gone on to develop outspoken classic basal-cell carcinoma. This, we feel, also supports the contention that basal-cell tumors are of hair origin and that trichoepithelioma and basal-cell carcinoma have a common genesis and are essentially the same lesion; the former merely is a maturer variant of the latter. Since we are satisfied that we can see in these basal-cell tumors all stages of development of hair from embryonal germs to outspoken hairs to actual formation of a hairy nevus, we feel that both these lesions are essentially hamartomas.

Stroma

Basal-cell carcinoma in at least some fields, in almost all tumors, grows or produces at its margins bulbous or bud-like nodularities that grow much in the fashion of and resemble, at least superficially, hair bulbs (Figs. 8 and 9). In many fields these "bulbs" or buds enclose or appear to "pinch" off small bits of stroma; this superficially resembles a papilla. This stroma often underwent basophilic, myxoid changes and liquefied. It was, in our experience, this change that most often gave rise to the adenoidal variant of this tumor and to the characteristic epithelial-tumor-mass retraction. Some tumors, however, did show vacuolation of individual cells or groups of cells; they resembled sebaceous-gland cells and were interpreted as changes in the direction of sebaceous glands. Some tumors had variable-sized areas of central necrosis. It is of interest to note that hair papillae will often undergo myxoid changes, particularly in areas of inflammation and in and about tumors of all kinds. The stroma, generally, of basal-cell tumors appears to grow with the epithelial portion of the tumor and to be an integral part of the tumor. The fibrous tissue around the epithelial nests of tumor

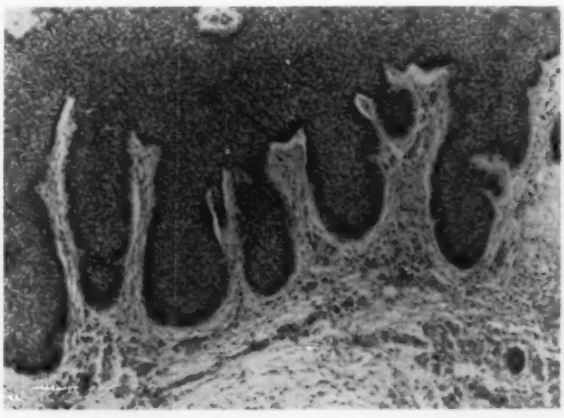


Fig. 8.—Characteristic surface "budding" or bulbs, enclosing the subtending dermis; × 100.

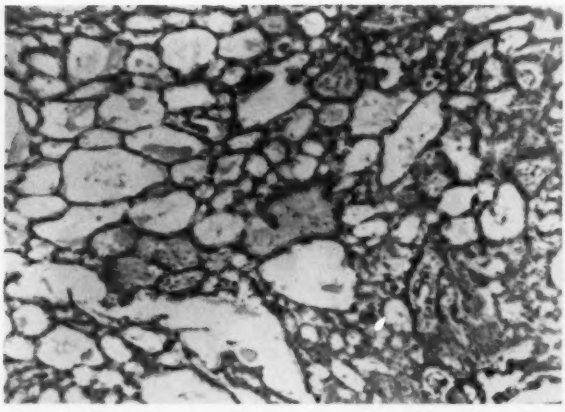


Fig. 9.—Enclosed stroma undergoing myxoid changes, and liquefaction producing adenoidal variant; × 100.

is loose, fibrillar, basophilic, and often very cellular. This is in contrast to tumors such as squamous-cell carcinoma, melanoma, or metastatic tumors, where the stroma only resists the invader and is finally torn apart.

This superficial resemblance of the stroma of basal-cell carcinoma to hair papillae and the follicular connective-tissue sheath was further investigated with the periodic acid-Schiff stain and toluidine blue in citric acid buffered to pH 5. These stains were used because the stroma of the papillae, the connective tissue sheath, and, to some extent, the outer sheath cells of growing hair follicles react positively with the periodic acid-Schiff reagent and stain metachromatically rather selectively with toluidine blue at pH 5 (Montagna). The papillae also contain alkaline phosphatase; I have not yet investigated the alkaline phosphatase content of the stroma of basal-cell tumors, although Kopf did find alkaline phosphatase in the stroma of 16 or 36 basal-cell tumors.

We found the stroma in the "pinched off," enclosed, and encircled areas in all the basal-tumors to be periodic acid-Schiff-reactive and, of even greater significance in all cases, to stain metachromatically. The great majority (271 lesions) stained intensely metachromatically, while some (18 lesions) stained faintly so (Figs. 10, 11, and 12). The controls included at least two examples of most skin lesions and larger numbers of the lesions listed earlier in the text. The controls generally were not contradictory but did raise some interesting questions. This control material will be reported in detail at a later time. There were areas

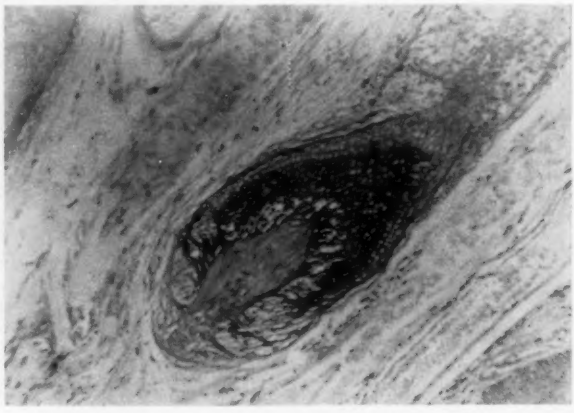


Fig. 10.—An active hair follicle, the "grayer" areas stained metachromatically with toluidine blue at pH 5. These areas include the papilla, outer connective tissue sheath, and, to a less extent, the outer sheath cells; × 100.

Fig. 11.—"Grayer" metachromatic stromal areas in a nest of basal-cell carcinoma; × 100.

of stromal metachromasia of varying degree in all the sclerosing hemangiomas, in some newly formed scars, in the stroma of the umbilical cord, interestingly about papillomas and carcinomas of the breast, around metastases of carcinoma of the breast, in areas in nevus unius lateris, in cylindroma, in cell borders of decidual cells, in fibrotic nodules in thyroid, and, of most importance, in a number of keratoses and particularly in all the seborrheic keratoses. This raises the question of the relationship of these keratoses to basal-cell carcinoma in that they have a common ancestor, the hair anlage. This is being further investigated. The metachromasia, interestingly, persisted in lesions blocked in paraffin for over a year. The toluidine blue also metachromatically unmasked the granulocytes and mast cells beautifully in two cases of urticaria pigmentosa. It was a revelation to realize the ubiquitousness of the mast cell in the skin.

The work of Wolbach is also of interest in this connection. He produced tumors in mice by stimulating the hair follicles with carcinogens after destruction of the papillae. His photomicrographs of the tumors produced resemble the keratoses in my control series, which I believe preliminarily to be of hair origin also.

The above "stromal" findings are, I feel, consistent with the tendency for basal-cell tumors to form not only hair but also its "stromal" components.

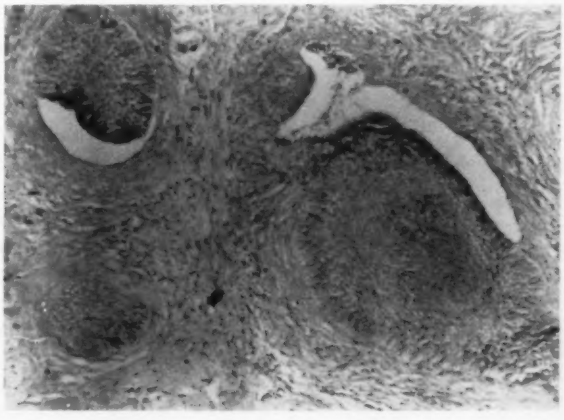
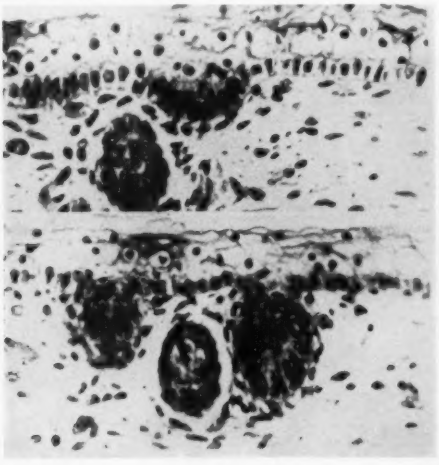


Fig. 12.—"Grayer" metachromatic change in subtending stroma about masses of basal-cell carcinoma; × 100.

Embryogenesis of Hair

I further investigated the embryologic development of hair, both in the literature and by study of the skin of various-aged fetuses. Briefly, hair in the human embryo and fetus develops first as a crowding proliferation and elongation of embryonal basal cells. This takes place in about the beginning of the third month of fetal life in areas like the eyebrows, upper lids, upper lip, and jaw and at about the fourth month over the body generally (see Arey). The continued crowding and proliferation of these basal germinative cells produces a bulge, which extends a bit up into the epidermis but soon begins to sink root-like into the dermis. This constitutes the primary epithelial germ bud. This primary epithelial germ continues to grow down into the corium and consists here of an outer layer of columnar basal cells and a central mass of cells proliferated from it. As the column grows downward, it takes with it a cord of epidermis. The tip of the downgrowing column becomes rounded, swollen, and finally "cup"-shaped, enclosing, or pinching off, or flowing around an altered mass of dermal mesenchyme which now forms the dermal papillae; it now constitutes the hair "bulb." The entire germ bud is surrounded by a mesenchymal envelope which grows and develops with the epithelial mass and which later forms the outer connective tissue sheath and the dermal papilla.

Fig. 13.—Primordia of hair follicles in the skin of a 5-month-old human embryo. The upper figure shows the primordia developing as a thickening of the basal layer of the epidermis. The lower figure shows a group of three slightly more advanced primordial hair follicles from the same embryo. (Reproduced with permission from Montagna, W.: The Structure and Function of Skin, New York, Academic Press, Inc., 1956.)



As the column grows downward, it acquires two lateral bulges. The proximal one later forms the sebaceous glands, and the distal, the bulge for attachment of the arrector pili muscle which is a site of high mitotic activity from which the hair may regenerate periodically (see below). The apocrine glands also develop as adventitious buds from this downgrowing hair follicle mass (Montagna).

The basal epidermal mass at the base of the bulb, from cells above the papillae (the hair matrix), continues to proliferate, and the proliferated cells, as a cord, push their way upward through the solid cord of cells and finally reach the surface and erupt. Above the level of the bulb, the cells begin to cornify, and they abruptly and finally form the dead keratinized hair. The upgrowing axial core of cells growing from the hair matrix differentiates into the inner sheaths, cuticle, cortex, and, where present, the medulla of the hair. The outer sheath is continuous with and is a downward extension of the surface epidermis (Figs. 13 and 15). Melanocytes occupy the upper portion of the bulb and are arranged as an inner cone surrounding the upper part of the dermal papillae (Kukita and Fitzpatrick). Whether these cells migrate from the neural crest and descend with the basal cells or are altered basal cells is not the problem to discuss here. The work of Kukita and Fitzpatrick on the demonstration of tyrosinase in melanocytes of the human hair matrix by autoradiography is interesting to me in light of the fairly frequent occurrence of melanin pigment in basal-cell carcinomas and other lesions I suspect of being of hair origin, such as the

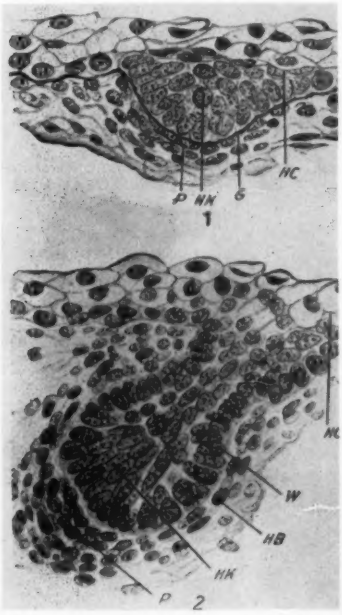


Fig. 14.—A situation similar to that of Figure 13; in diagram, *P* is the primordium of the papilla. (Reproduced with permission from Maximow, A. A., and Bloom, W.: A Textbook of Histology, Ed. 4, Philadelphia, W. B. Saunders Company, 1942.)

seborrheic keratosis. They demonstrated that the melanocytes of human black hair matrix had an uninhibited, actively functioning tyrosinase system, while the epidermal melanocytes have an inhibited tyrosinase system (Fitzpatrick, Becker Jr., Fitzpatrick, and Montgomery and Fitzpatrick and Kukita). These facts, they point out, are in agreement with the clinical findings of heavily melanized (black) hair and a coexistent white skin. It should be pointed out that the embryogenic events are dynamic and continuing and that many of the changes go on at the same time or one event just gradually becomes the next.

It also seemed to us that in the skin of the 2- to 3-month-old fetus a condensation of dermal stromal cells often appeared below the epidermis without any evident change in the overlying stratum germinativum. A similar condensation and alteration of polarity of dermal cells appeared beneath obvious beginning and developing hair germs. This raises the question as to whether the anlage of the papilla forms first and then in some way induces or paves the way for the formation of the downgrowing epithelial germ bud. This is interesting to us, since there is some evidence that the papilla is a determiner of hair growth and development in pre- and postnatal life as well. When hair duplication occurs, as in pili multigemini, there is a corresponding duplication of the dermal papilla (Pinkus [1951] and Montagna); Wolbach showed that a hair will continue to regenerate as long as the papilla is not destroyed, no matter how severely injured it is.

We compared the development of the hair with basal-cell carcinoma and found strik-

Fig. 15.—Four stages in the development of hair follicles, from the skin of a 5-month-old human embryo. On the left is a primordial cord of cells growing from the epidermis. In the next diagram, the cord of cells has become longer and has developed an upper and lower swelling which will differentiate, respectively, into sebaceous glands and hair bulge. The condensation of mesenchymal cells at the base of the cord will be dermal papilla. A cone of inner sheath (left unstippled) has formed above the bulb. The tip of this cone is pushing its way through the cord. Behind the inner sheath is the tip of the growing hair (drawn solid black). A connective tissue sheath is beginning to differentiate around the follicle. The follicle on the extreme right is fully formed. (Reproduced with permission from Montagna, W.: The Structure and Function of Skin, New York, Academic Press, Inc., 1956.)

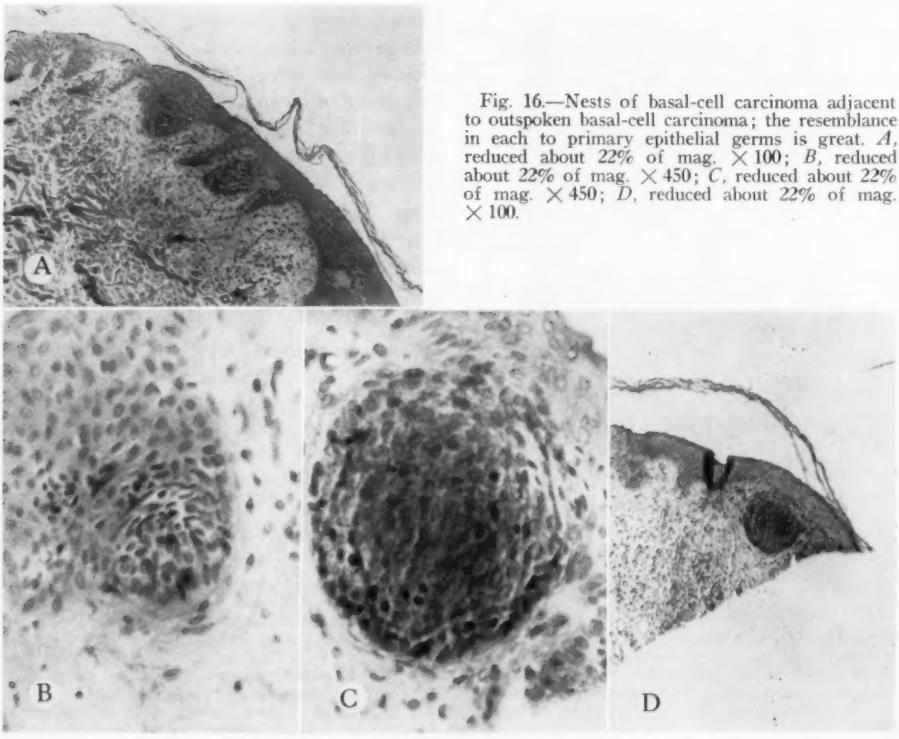


Fig. 16.—Nests of basal-cell carcinoma adjacent to outspoken basal-cell carcinoma; the resemblance in each to primary epithelial germs is great. *A*, reduced about 22% of mag. × 100; *B*, reduced about 22% of mag. × 450; *C*, reduced about 22% of mag. × 450; *D*, reduced about 22% of mag. × 100.

ing similarities between these two events, from the earliest inception of crowded hyperchromatic basal cells, through proliferation of these cells and the formation of the primary epithelial germ, to hair bulb, to matrix, and, finally, to inner and outer sheaths (Figs. 6 to 9).

The undifferentiated superficial basal-cell carcinoma and some areas in more bulky, penetrating, older, infiltrating tumors particularly resembled the primary epithelial germ evident in the skin of the 3- to 4-month-old fetus. It was our impression that basal-cell tumors develop as do hairs embryologically, that they recapitulate the embryonic development of hair, that hair anlage and basal-cell carcinoma anlage or "potential" reside in a basal or germinative cell with potential for forming hair at any time "built in," and that the final or given pattern of the tumor at any time depends on just how far the hair germ has developed or matured or perhaps at what stage its development has been arrested. Lever, again, feels that the pattern is dependent on the degree and direction of differentiation in the primary epithelial germ prior to the onset of neoplasia.

Basal-cell tumors, also, not infrequently occur with other "tumors" also presumably of primary-epithelial-germ origin. I have studied one case of a large sebaceous nevus of Jadassohn in a 9-year-old boy in which there was a focus of evident basal-cell carcinoma showing, incidentally, "keratin-whorls" or changes interpreted as being in the direction of hair follicles.

Genetic factors (Bissel, Thigpen) also appear to be a factor in basal-cell tumors as well as in hair growth and distribution. Goldman, as well as others, discusses the genetic aspects of trichoepithelioma, and Oettle recently described a situation in which three of four brothers, at a relatively early

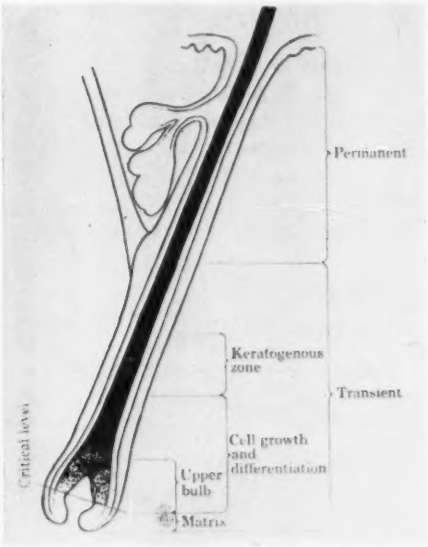


Fig. 17.—The transient zone of the follicle completely disappears, and, from the outer sheath of the upper or permanent portion of the follicle, an entirely new hair follicle develops, recapitulating hair embryogenesis. (Reproduced with permission from Montagna, W.: The Structure and Function of Skin, New York, Academic Press, Inc., 1956.)

age, developed basal-cell carcinomas. Two of the brothers were identical twins and developed their lesions at the same spot.

Postnatal Growth, Replacement, and Regeneration of Hair

We then looked to the hair itself for clues to the genesis of these tumors; we wanted to know whether new hair germs ever formed during postnatal life and, if so, from where and what stimulated them. We also wanted to know for how long new hair germs would form, if they ever did form; for how long could the anlage of these germs maintain their hair-raising potential? Was there anything in the life history of the hair that would suggest easy derangement and possible tumor formation? Our study was from literature and skin obtained surgically and at necropsy. We found that the hair and its related supporting structures undergo cyclical changes all during life. There is a building up and tearing down of a complex structure, a period of rest, and then the formation of a new hair; we found that the hair is an elaborate balanced structure that even minor deviations from the norm could unbalance (Pinkus, Montagna). Here was indeed a structure that seemed to us at least vulnerable to easy derangement and possible "tumor" formation of the hamartomatous type seen in basal-cell carcinoma.

Regeneration, with gradual and continuous replacement of the shed hair, is a normal process that goes on all over the body all through life, fetal and postnatal, and is clinically obvious in the shedding of lanugo hairs and their replacement with thicker hairs, in hair growth at puberty, and in hirsutism.

The lower half of the follicle (Montagna) (Figs. 17 and 19) is a transient structure which disappears as the hair ceases to grow and is shed. The outer sheath of the upper portion of the follicle, as mentioned above, which is a derivative and downward extension of the surface epidermis, forms an epithelial sac, lined by the altered inner sheath, around the resting or club hair, and from this outer sheath a new hair germ

Fig. 18.—Hair follicles from the scalp. On the right is the bulb of an active follicle; on the left is the lower part of a follicle during catagenesis. In the upper right-hand corner of this figure a club hair is being formed; the matrix is completely degenerated, and the dermal papilla is being released. The vitreous membrane around the degenerating bulb is very thick. (Reproduced with permission from Montagna, W.: The Structure and Function of Skin, New York, Academic Press, Inc., 1956.)

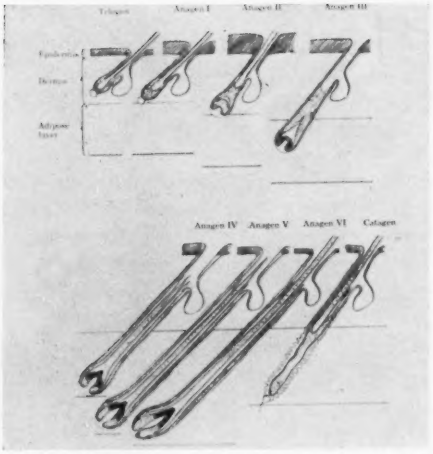


Fig. 19.—The growth cycle of the hair follicles of the mouse (drawn to scale). Observe that the epidermis becomes increasingly thicker in the early stages of (growth) anagenesis. The dermis and adipose layer become thickened after Anagen III. (Reproduced with permission from Montagna, W.: The Structure and Function of Skin, New York, Academic Press, Inc., 1956.)

arises. From this new hair germ, there arises, just as in embryonic development, an entirely new hair with all of its component parts: matrix, bulb, root sheaths, and shaft. The new germ presents as a cord of cells extending down from the outer-sheath epithelial sac to the hair papilla. There is some controversy as to whether an entirely new germ forms and whether it forms from outer sheath cells with a "built in" potential. Some observers believe that some of the matrix persists and that from this persistent matrix which overlies the papilla a new follicle forms. It was our feeling that the entire lower half of the follicle perished and an entirely new germ formed from outer sheath cells. I asked this question of Dr. William Montagna, and he replied that he believes that the cells in the cord below the epithelial sac about the club hair (which constitutes the new germ) are mostly derived from the outer root sheath in the upper half of active hair follicles. The matrix perishes during catagenesis, and if any part of it is left it has eluded him. He wrote that he followed this phenomenon very carefully, particularly by treating skin with x-rays, and that he is convinced that no trace of the matrix is left at the completion of catagenesis. These cells, then, he believes, are derived from the outer root sheath and have undergone a retrograde type of differentiation, and they can behave like primordial cells.

The activity in regeneration or regrowth appears to begin in the papilla, which is thought to persist, although a new one may form from either new or persistent stromal cells (this is controversial and undecided; see Wolbach). The papilla contacts the cord of cells, the new hair germ, from the outer sheath of the club, or resting hair, and a new hair begins to grow.

Similar changes occur or can be induced by plucking of the hair or after x-ray epilation and were seen in the scalps of Hiroshima atom-bomb victims (Liebow). A good deal, I feel, could be guessed about the etiology of basal-cell tumors if we knew what controlled the proliferative activity of the cells of this upper outer sheath of the epithelial sac of the hair follicle. It is interesting and perhaps significant to note Foot's observation that basal-cell tumors originate from the upper part of the follicle. Pinkus has made the suggestion that the hair-growing potential may reside in the lower bulge to which the arrector pili muscle attaches.

There is good evidence in animals—rats, mice, guinea pigs, rabbits—and some admittedly tenuous evidence in humans that entirely new hair germs and follicles will form or regenerate from newly formed or regenerated epidermis (see Medewar, Ribbert, Silberberg and Silberberg, Taylor, and Planner), provided that the dermal tissue underlying was either the old dermis or that the newly formed dermis was completely differentiated or highly vascularized, with abundant granulation tissue. The inference here is that the dermis furnishes either an inductive factor or a suitable bed for the hair germ to develop and grow in. This is interesting in the light of the work of Wolbach, mentioned above, in which he showed

that a follicle deprived of its papilla or papilla cells no longer forms follicles, only epithelium and sebaceous glands, and that permanent epilation occurs only when the dose of x-ray has been sufficient to damage the dermal papilla.

Butcher, with underfeeding experiments in mice, showed that hair-forming potential resides in the stratum germinativum for long periods; Hardy, in tissue culture studies, showed that the dermis and epidermis of mice are capable of forming and maintaining hair follicles independent of other obvious factors, cellular, circulatory, or nervous. From this it appears that the epidermis and dermis have a "built in" potential for the formation of hair, and this suggests that the organogenetic factors are deposited in the skin and reside there until needed before the morphogenetic differentiation of the follicle takes place. That the hair, even in the adult, is a labile structure (Allen) is evidenced by the unsuccessful attempts in alopecia areata, for example, at hair regeneration in the form of epithelial buds along the follicle and accumulation of keratinous debris of abortive hair shafts in the follicular ostia and by the various changes hair will undergo in areas in and adjacent to inflammations and tumors (Haythorn), even to changes mimicking basal-cell carcinoma. A follicle may produce more than one kind of hair, seen, as mentioned, in the change from lanugo hairs, at puberty and in hirsutism. We have seen new primary epithelial germs developing in keratoses of various sorts and have seen bud-like projections resembling primary epithelial germs sprouting from cystically dilated, keratin-plugged hair follicles. Felix Pinkus observed a single follicle on a precisely identified spot on the back of the right hand for a period of six years. During this time it gave rise to 12 hairs. The average life span of each hair was 180 days, but the actual length of life differed considerably. All the hairs under observation were different; each presented highly individual characteristics.

Conclusion

We are left with the feeling that basal-cell carcinoma is an example of oncogenesis recapitulating embryological development; that these tumors are an aberrant exaggeration of normal hair development, cyclical regrowth, and regeneration; that the various patterns and forms of basal-cell carcinoma are dependent upon just how far this development or regrowth has gone or has been arrested; that these tumors are derived from the cellular primordia of the hair, which we believe is a basal cell with "locked-in" hair-forming potential, influenced in some way by the dermis, where in truth the potential may actually be "locked," and that in the cyclical life of the hair, with its constant degeneration, regrowth, and continuous production of new germs, there is ample opportunity for derangement and formation of tumors of the basal-cell hamartoma type.

If any of this is valid at all, then there is in the study of hair and the many factors that influence its growth and development (see Allen, Montagna, and Baker) a good tool for the study of the etiology of basal-cell carcinoma. Admittedly, much needs experimental substantiation, and I am in the midst of trying.

Summary

The histogenesis of basal-cell carcinoma is reviewed. Tangential evidence from a morphologic study of 291 basal-cell carcinomas, epithelium and stroma, trichoepithelioma, and normal and fetal skin and a morphologic comparative study of these tumors with the embryogenesis and histogenesis of hair growth, replacement, and regeneration is presented in support of the contention that basal-cell tumors are hamartomas and take origin from hair anlage.

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Subcorneal Pustular Dermatosis

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Introduction

In December, 1956, Sneddon and Wilkinson[1] described six patients who had a bullous dermatitis which resembled dermatitis herpetiformis in many of its clinical features but which was characterized by the presence of subcorneal pustular vesicles. They believed that these patients had a distinct and new syndrome and used the name subcorneal pustular dermatosis.

Five of their six patients were female. Their ages ranged between 41 and 68 years and the disease had persisted from three months to nine years. Characteristically, the axillae, groin, abdomen, and flexor aspects of the proximal parts of the limbs had been affected by recurrent waves of milky or pustular vesicles which formed irregular groups of annular or gyrate lesions. The individual lesions often appeared on a slight erythematous flare, were oval, rapidly increased in size, became flaccid, and dried to form a very thin superficial crust. A reddish stain or hyperpigmented macule was left as a residual of the vesicles. A marked therapeutic benefit was achieved with sulfapyridine in one of the patients, and the other five were benefited with diaminodiphenyl sulfone (Dapsone).

Since dermatitis herpetiformis is a somewhat polymorphous bullous disorder, in that it may be represented by a few scattered pruritic pustules or by an extremely extensive fulminate bullous disease, the histologic appearance of a typical vesicle of dermatitis herpetiformis in the subepidermal position has been used as an important diagnostic criterion. Therefore, the recognition of cases clinically similar to dermatitis herpetiformis but in which the vesicle was subcorneal rather than subepidermal suggests that a distinctly different disorder or an important subdivision of dermatitis herpetiformis is represented.

During the past four years three instances of atypical dermatitis herpetiformis were encountered in The Johns Hopkins Hospital. In light of the study of Sneddon and Wilkinson, these cases were reviewed, and, because of the clinical similarities to dermatitis herpetiformis and the histologic presence of a subcorneal blister, they are considered to be similar to the cases of the English authors.

CASE 1.—A 75-year-old Negro woman attended the outpatient department of The Johns Hopkins Hospital in April, 1955, because of a pruritic, vesicular eruption which had involved the lower trunk and legs for one year. Her parents had died at ages 84 and 94, and many siblings had lived to an old age without developing any skin disorder. The patient experienced no significant illness until 1952, at which time she was found to have hypertension. This was thought by her examining physician to be related to the severe emotional stress encountered in her home situation. During the year preceding her visit to the clinic, she experienced recurrent bouts of pustules developing on the legs. She denied taking any medicines or drugs. Physical examination revealed a well-developed, somewhat thin, elderly Negro woman who did not appear to be acutely ill. The blood pressure was 180/110 mm. of mercury. The pulse rate was 114/min. Randomly scattered over all aspects of the legs were vesicles and pustules and involuting, crusted vesicles. The skin was otherwise not remarkable. There was slight enlargement of the heart and an occasional premature ventricular contraction. The remainder of the physical examination was not remarkable. Laboratory studies at that time included a hematocrit value of 45%. The erythrocyte sedimentation rate was 32, corrected to 29 mm. per hour (Wintrobe), the white blood cell count was

Submitted for publication June 28, 1958.

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8600/cu. mm. with a normal differential cell count. Blood nonprotein nitrogen and blood sugar values were normal. The urine contained a trace of albumin but was otherwise negative. A clinical diagnosis of bullous impetigo was made and a biopsy specimen of a fresh blister was obtained. The biopsy was interpreted as showing changes compatible with the diagnosis of impetigo. Local hygienic measures and therapy with 3 gm. of sulfisoxazole (Gantrisin) daily was instituted. Some clearing occurred, but during the next year repeated crops of vesicles appeared on the legs and trunks. Bacteriologic cultures made from the vesicles revealed beta Streptococcus and hemolytic Staphylococcus aureus on one occasion. Penicillin and chlortetracycline were administered systemically, and tetracycline ointment was applied locally, without benefit. In the fall of 1956, sulfapyridine therapy was instituted and was accompanied by a temporary remission. By March, 1956, crusted, annular, and gyrate lesions had developed over the trunk and legs. This eruption was thought by the examiner to resemble dermatitis herpetiformis. In April, 1957, a similar annular and gyrate eruption involved the axillae as well as the legs. Potassium arsenite (Fowler's) solution N. F. and intramuscular penicillin were used without essential change in the lesions. A second biopsy specimen of a vesicle from the leg was obtained, and the previous biopsy specimen was reexamined.

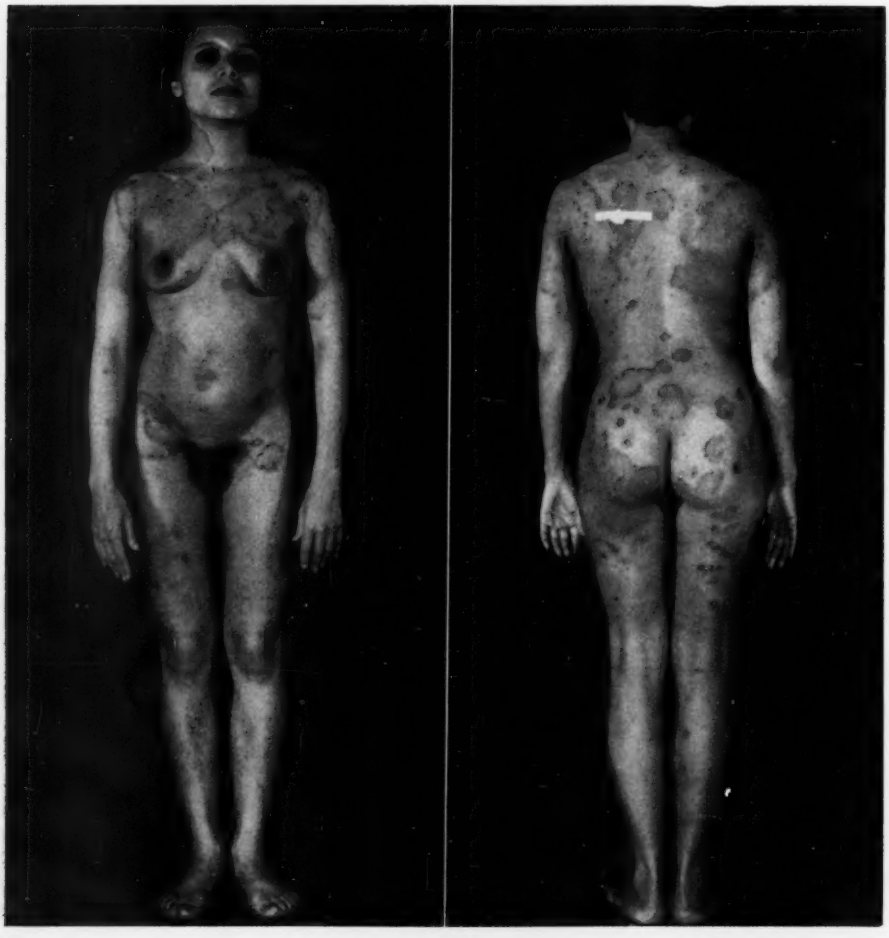
Pathology.—A section from the first biopsy specimen revealed a subcorneal vesicopustule approximately 3 mm. in diameter. The vesicle cavity was about 200μ deep and contained a pustular layer approximately 100μ thick. The granular layer of the rete formed the base of the vesicle. The rete was half its normal width, and on the surface were a few exfoliative epidermal cells which had a few poorly developed prickles. The cell nuclei showed partial condensation. There was a moderate inter- and intracellular edema of the epidermis with mild exocytosis. In the upper cutis there was mild edema and a perivascular infiltrate consisting predominately of mononuclear cells with a few polymorphonuclear leukocytes and eosinophils. Sections from the second biopsy revealed a vesicle with a very thin keratin layer elevated approximately 0.5 mm. above the surface of the granular layer which formed the base of the vesicle. A layer of cellular debris approximately 100μ thick occupied the vesicle cavity. On the epidermal surface were a few rounded epidermal cells without prickles, with well-defined borders and twice as large as the normal rete cell. They were rounded, contained a moderately dense cytoplasm, and had a slightly enlarged, deeply-staining nucleus. No space or thinning of the cytoplasm about the nucleus was present, and the cells resembled corps ronds (or Tzanck-like cells). There was a mild edema and exocytosis involving the epidermis, and in the upper part of the cutis was a very mild edema and perivascular infiltrate consisting predominately of mononuclear cells. Some of the small capillaries were filled with polymorphonuclear cells without any vascular endothelial change. It was felt that the thinness of the keratin layer overlying the vesicle, the moderately large size of the vesicle and the sparse layer of leukocytic debris occupying the cavity, and the moderate to mild inflammatory reaction in the epidermis and cutis were points against the diagnosis of impetigo and suggested subcorneal pustular dermatosis.

CASE 2.—A 44-year-old Negro woman was first admitted to The Johns Hopkins Hospital in July, 1954, complaining of severe left flank pain of approximately eight days' duration. The family history was noncontributory. A diagnosis of syphilis was made in 1930, and a protracted course of heavy metal therapy was administered. She had also received penicillin on a number of occasions for other causes. She had experienced four pregnancies and had three living children. The review of systems was not otherwise remarkable. One week prior to admission to the hospital progressively severe cramping pain developed in the left costovertebral angle. During the same period of time, erythematous papules and vesicles appeared over the legs and the lower part of the trunk. Upon admission to the hospital, the blood pressure was 130/90 mm. of mercury, the temperature was 98 F, and the pulse rate was 60/min. The patient did not appear acutely ill. Over the trunk, arms, legs, and particularly in the intertriginous areas were numerous tense and flaccid vesicles and evidence of excoriation. Some lesions contained milky fluid, and others were frankly pustular. There were two left cervical, firm, nontender lymph nodes. The ears, nose, and throat were normal. The chest was clear. The heart was not enlarged, and no cardiac murmurs were heard. There was abdominal tenderness to percussion or pressure in the left costovertebral angle. The liver and spleen were not felt. The external genitalia were normal, as were the pelvic organs. The serologic test for syphilis was negative. The hemoglobin was 12 gm. per 100 ml. of blood, and the white blood cell count was 5600 per cubic millimeter. Serum nonprotein nitrogen, calcium, and phosphorus were normal. Serum albumin was 4.3 and the globulin 3.3 gm. per 100 ml. Urinary studies reveal a nonfunctioning left kidney. Accordingly, on the fourth hospital day a left nephrectomy and left partial ureterectomy were performed, with removal of a small, atrophic left kidney with evidence of hydronephrosis and chronic pyelonephritis. A left ureteral calculus was also discovered in the operative specimen. Hemolytic S. aureus was

cultured from the kidney and from a wound infection in the operative site. The patient was treated with 6 gm. of sulfisoxazole and 1 gm. of tetracycline a day for the remaining 10 days of hospital stay. The vesicular eruption was somewhat improved during this period of therapy.

After discharge from the hospital the patient attended the dermatology clinic, where a biopsy of a vesicle was performed and a culture of vesicle fluid was obtained. The clinical impression at that time included generalized herpes simplex or bullous impetigo. The culture of the vesicular fluid on that occasion and when repeated two years later was sterile. The biopsy findings were interpreted as compatible with impetigo. Therapy consisting of tetracycline, 1 gm. a day, and local hygienic measures, was instituted. During the following year the vesicular eruption varied widely in extent from a generalized distribution, sparing the hands, feet, and face, to an almost total absence of any lesions. The patient did not attend the clinic for two years, and upon her return in December, 1957, she reported that episodes of a vesicular and very pruritic eruption had recurred during the previous two years. At that time there was widespread eruption over the trunk, forearms,

Figs. 1 and 2 (Case 3).—Light-colored Negro woman, aged 25, who had had subcorneal pustular dermatosis for five years. The eruption was still active three years later. The photographs show the general configuration and distribution of the lesions and the tendency for the lesions to extend from the intertriginous areas, forming fairly large plaques with narrow vesicopustular borders. The face and lower parts of the extremities are essentially clear. Three years after the photograph was taken the plaques were of relatively smaller size; none were over 4 or 5 cm. in diameter and the intertriginous feature was missing.



upper legs, back, and the sacral triangle. This consisted of small, 2 to 5 mm., vesicles and intermingled hyperpigmented macules. A second biopsy was obtained and because of the clinical impression of dermatitis herpetiformis, therapy with sulfisoxazole, 2 gm. a day, was instituted and was followed by marked clearing of the vesicular lesions. Therapy was continued sporadically during the next four months, and in April, 1958, further specimens for biopsy were obtained from vesicles. At this time sulfapyridine, 0.5 gm. four times daily, was administered, and within two weeks all of the lesions had disappeared. During the years 1954 to 1957 urine cultures had revealed hemolytic Staphylococcus albus and gamma Streptococcus on three occasions and Escherichia coli on a fourth. The hematocrit value and white blood cell counts remained entirely normal. On three occasions, the erythrocyte sedimentation rate had been determined and was increased to approximately 34 mm. per hour (Wintrobe).

Pathology—A biopsy section from a vesicle on the abdomen revealed a 3 mm. vesicle with a cavity 5 mm. in depth. A thin layer of polymorphonuclear leukocytes, debris, and serum was present on the upper surface of the epidermis. The epidermis was involved with moderate intra- and intercellular edema, and it was slightly thickened. The upper cutis contained a very light infiltrate of small mononuclear cells, and the capillaries were slightly dilated. The second biopsy specimen from the abdomen showed a similar subcorneal vesicle approximately 200μ in depth. The epidermis underlying the vesicle cavity was edematous. Several tiny subepidermal vesicles were present, the largest of which was approximately 200μ in diameter. A perivascular infiltrate, somewhat heavier than in the first biopsy, was present. Sections of a third biopsy revealed a very thin keratin layer forming the vesicle roof and a thin zone of dried serous cellular debris. The epidermis contained intra- and intercellular edema. The cutis contained a narrow band-like perivascular infiltrate consisting predominately of small mononuclear cells. In a fourth biopsy specimen there was a larger drying subcorneal pustule with more edema in the cutis, and the papillary layers of the epidermis and a few of the upper epidermal cells seemed to be exfoliated and to have lost their prickles. All of the sections were thought to show changes compatible with a diagnosis of subcorneal pustular dermatosis.

Case 3.—A 27-year-old Negro woman first attended the dermatology clinic of The Johns Hopkins Hospital in October, 1955, because of a rash which had involved the neck, arms, and legs for approximately five years. The family history was not remarkable. Her general health had been good. Usual childhood diseases had been experienced without difficulty. At age 3 years several enlarged cervical nodes had been surgically drained. Mild bronchitis had recurred at frequent intervals. Roentgenograms of the chest at intervals throughout her life were said to be negative. She had experienced two pregnancies and had two living children. With each pregnancy, the patient was told that she was anemic. In 1951, groups of blisters had appeared in both axillae, and during the ensuing years pruritic groups and single blisters formed over the upper part of the chest and progressively involved the trunk and the extremities but had spared the face, hands, and feet. Specimens for biopsy and scrapings of the skin had been obtained on several occasions, and therapy had consisted of sulfonamides, ultraviolet light, and other, unknown, medications. She was presented before the Baltimore-Washington Dermatologic Society on several occasions. Therapy with sulfonamides had repeatedly ameliorated but had not cleared the vesicular eruption. At the time of her visit to the clinic, the chest, the axillae, the deltoid regions, the back, and inguinal regions were involved with extensive gyrate lesions with concentrically arranged, serpiginous borders. The borders consisted of fresh and involuted crusting vesicles and pustules approximately 2 to 4 mm. in size. In addition, single vesicles were scattered over the trunk. Numerous hyperpigmented macules, in various stages of drying, were present. The remainder of the physical examination was not remarkable. The hematocrit value was 29%, the hemoglobin was 7.9 gm. per 100 cc. of blood, and the icterus index was 5. The white blood cell count was 5800 per cubic millimeter, and the differential cell count was normal. Examination of the blood smear revealed a moderate degree of microcytosis and hypochromia. The urinalysis was normal. A roentgenogram of the chest was normal. Scrapings of vesicles on several occasions did not yield any fungus growth. A culture obtained from one of the vesicles revealed hemolytic S. aureus. A biopsy was interpreted as suggesting impetigo much more strongly than dermatitis herpetiformis because of the subcorneal location of the vesicle. The clinical diagnosis of dermatitis herpetiformis was made, however, and therapy with 3 gm. of sulfapyridine a day was instituted. Improvement occurred, but the lesions did not clear completely. In 1956, 3 gm. of sodium 4,4'-diaminodiphenylsulfone-2-acetylsulfonamide (Promacetin) a day was administered, and this therapy was followed by a decrease in the severity of itching. In February, 1956, the patient complained of dysuria and urinary frequency. Examination of the urine revealed no leukocytes, and a urine culture at that time was sterile. The skin eruption had become extensive, and therapy with potassium arsenite solution N. F. was instituted. During the next two years the

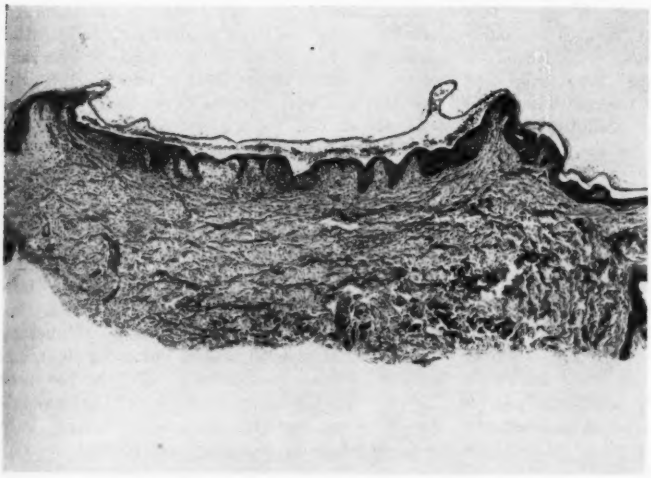


Fig. 3 (Case 3).—A section shows one of the vesicopustules (×35). There is a thin keratin layer elevated above the epidermis. Above the granular layer there is a relatively thin layer (about 100μ) of pus, consisting mostly of leukocytes. The epidermis is somewhat acanthotic and shows moderate exocytosis and evidence of edema. In the center are two large dermal pegs which show more edema. In the upper cutis there is a light subacute infiltrate that tends to be perivascular.

patient managed her own therapy at home with sulfapyridine, using 1 to 3 gm. per day depending upon the severity of the vesicular eruption. By this means she was able to control the severest itching and to keep the eruption from becoming widespread. However, at no time was she completely free of vesicular lesions. In 1958 the patient returned to the clinic for examination. She appeared to be in good health. The blood pressure was 120/80 mm. of mercury. The temperature was 98 F. The pulse rate was 80. The skin was pigmented in a normal fashion for a Negro but was of a very light tone. Scattered over the trunk, upper legs, and arms were numerous hyperpigmented macules, some of which were slightly atrophic in the center. Over the anterior chest, in the axillary region, on the lateral chest, and over most of the back were grouped and individual vesicles in various stages of evolution. The mucous membranes were pale. The remainder of the physical examination was not remarkable. The hematocrit value was 29%. The icterus index was 5. The white cell count was 6300 per cubic millimeter, and the differential cell count was normal. The erythrocyte sedimentation rate was normal. No sugar, albumin, or leukocytes were present in the urine. A vesicle was carefully ruptured and cultured, but no growth was obtained. Electrophoresis of the serum proteins revealed a mild decrease in the alpha globulin fraction. Biopsy of fresh lesions were obtained.

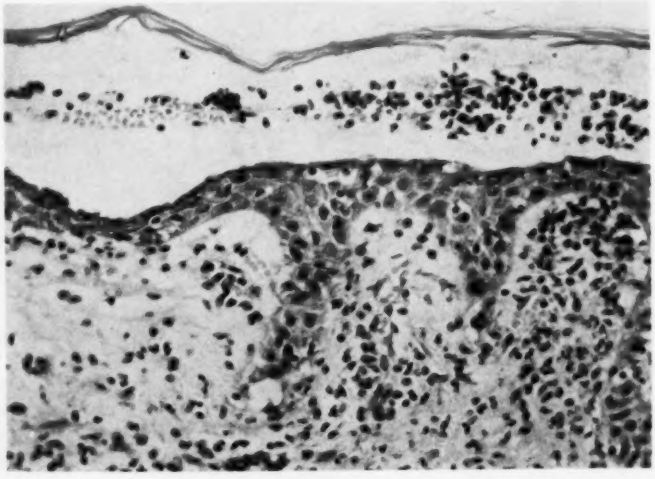


Fig. 4 (Case 3).—A higher magnification (×300) of the two large, edematous dermal pegs from Figure 3. An unusual degree of edema beneath the epidermis approaches the picture of a subepidermal vesicle. The exocytosis and mild infiltrate are clearly seen.

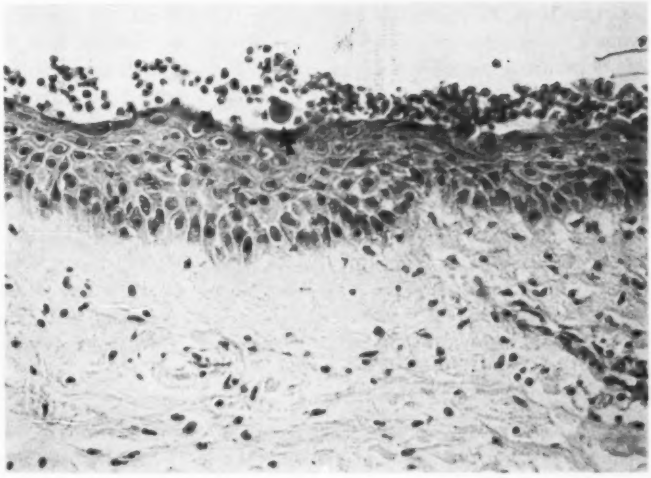


Fig. 5 (Case 3).—Magnification of 300 × shows the thin layer of polymorphonuclears and several acantholytic cells at the base of the vesicle. In the center there is one large isolated acantholytic cell (arrow), and to the right of this are several others that are apparently still attached to the upper layers of the rete. This slide demonstrates well the usual lack of edema in the epidermis and in the dermis, and the light infiltrate in the upper cutis.

Pathology.—In each of the three biopsy specimens examined a subcorneal vesicle was present with a thin keratin roof and with a granular layer of the epidermis forming the base. In each of the three, a pustular exudate was present within the vesicular cavity. The epidermis was involved with edema and exocytosis. In one section minute subepidermal loculated vesicles were present. The upper cutis of the three specimens contained a mild mononuclear infiltrate, slight edema, and vascular dilatation. The biopsies were thought to show changes compatible with the histologic diagnosis of subcorneal pustular dermatosis.

Comment

Since the etiology and pathogenesis of dermatitis herpetiformis are not known, the term dermatitis herpetiformis remains descriptive at best. However, many years of experience with the disorder have indicated that the features of the syndrome are relatively constant, consisting essentially of intense pruritus, grouped vesicles recurring for many years on the trunk and extremities, seldom involving the mucous membranes, and often presenting in gyrate or arcuate configurations. An unusual sensitivity to iodide has frequently, but by no means invariably, been present, and a therapeutic response to sulfonamides, particularly to sulfapyridine, has been a valuable diagnostic point.

The term subcorneal pustular dermatosis has been coined to describe cases in which the clinical features are almost identical with dermatitis herpetiformis but in which the subcorneal vesicles are virtually indistinguishable from those of impetigo. It is inevitable that some persons will consider this syndrome to be a subcorneal form of dermatitis herpetiformis; others, an infectious or impetigoid disease, and a third view will be shared by those who believe that a new disorder has indeed been delineated.

Data on 14 cases which present similar clinical and histological manifestations are available for study. This includes the six cases of Sneddon and Wilkinson; 1 each reported by Hellier,[2] Carney,[3] Cipollaro,[4] Burgoon et al.,[5] and Greenbaum and Lee[6] and three cases in the present report. When these cases are considered together, the clinical picture remains remarkably like that described by Sneddon and Wilkinson. Dr. H. Beerman presented a histologic section from a case of subcorneal pustular dermatosis before the Clinical Pathological Conference of the American Academy of Dermatology in December, 1957. There may be some doubt that Hellier's[2] case belongs strictly in this group because of the distribution of the eruption and because of the morphology of the vesicopustules.

Four of the patients in this group of fourteen were male and only one was

younger than 40 years. A predilection for women is in contrast to the high incidence of dermatitis herpetiformis in men. The intertriginous areas, particularly the axillae, were the sites of individual and bizarrely patterned vesicles in many members of this group. Such gyrate configurations are not uncommon in cases of dermatitis herpetiformis, but in that disorder the intertriginous areas are seldom involved. The pattern of lesions in Patient 3 of this report is also similar to the pattern encountered in erythema multiforme or in erythema annulare centrifugum.

Two of the three patients reported on in this article have experienced recurrent urinary difficulties, and in one of these urinary tract infection was clearly demonstrated. Staphylococcus and hemolytic Streptococcus were cultured from the vesicle fluid of one patient, although on another occasion the vesicle fluid was sterile. In another member of the group, the vesicles were culturally negative on two occasions. Many workers have suggested that dermatitis herpetiformis may be related to recurrent and chronic focal infections. The possible relationships between the vesicular eruption and the infection has not been stressed in reported cases of subcorneal pustular dermatosis. The evaluation of sulfonamide therapy in the presence of urinary tract infection is difficult, since the improvement may be related to the effect of the bactericidal agent on the infection or may result from the nonbactericidal effect of sulfonamides on the underlying process responsible for formation of the vesicles. Pruritus has not been stressed in previously reported cases of subcorneal pustular dermatosis. In all three of the cases reported here pruritus was intense, and upon several occasions it was relieved after sulfapyridine therapy, although the vesicles continued to appear. The therapeutic effectiveness of sulfonamides and the sulfones cannot be evaluated accurately among these patients, since the dosage, the duration of therapy, and the criteria of satisfactory benefits were in no way standardized. One of the patients of Sneddon and Wilkinson was said to have responded to sulfapyridine. The patient reported by Carney [3] had no relief after six days of therapy with sulfapyridine, but this short course of therapy makes evaluation particularly difficult. The patient of Burgoon et al.[5] did well with this treatment. Complete clearing of the vesicles occurred in one of the three patients reported here. In a second, benefit could be increased by increasing the daily intake of sulfapyridine from 2 to 4 gm. a day. Such disparate therapeutic results also characterize the therapy of dermatitis herpetiformis.

The clinical course of all of the 14 cases is clearly distinguishable from that of impetigo. The disorder appears in a much older age group than is usual for impetigo, the vesicles are frequently sterile, and the distribution and size of these vesicles is far more extensive than in impetigo. Furthermore, impetigo is characterized by marked contagiousness, which is not true of the cases forming the present group. Finally, the clinical response to penicillin and tetracycline which typifies impetigo is not apparent among these cases.

Vesicles of dermatitis herpetiformis, erythema multiforme, and bullous pemphigoid are characteristically subepidermal in location and can be readily distinguished from the subcorneal vesicles.

In most of the sections studied only subcorneal vesicles were encountered. However, in an occasional biopsy specimen minute loculated subepidermal vesicles have been found in cases which have been considered instances of subcorneal pustular dermatosis. No observations are available which will allow a correlation between this type of vesiculation and the subepidermal vesiculation characteristic of dermatitis herpetiformis.

Therapy of these subcorneal vesicular disorders has not been uniformly successful with any one of the sulfonamides or sulfones. Although, within the group, as within the group of dermatitis herpeti-

Reference Case	Sex	Age, Yr.	Duration, Yr.	Involved Region	Description of Lesions	Histological Characteristics	Therapy
1. Sneddon & Wilkinson Case 1	F	51	2	Neck, shoulder, arms, breast.	Circinate, gyrate groups of vesicles and vesicopustules	Subcorneal vesticle with PMN exudate mild inflammatory changes	Sulfapyridine
2. Sneddon & Wilkinson Case 2	F	65	6	Abdomen & thighs	Circinate, gyrate vesicles	Subcorneal vesicle as above	Dapsone
3. Sneddon & Wilkinson Case 3	F	54	1	Back axillae, groin, chest	Annular grouped vesicles & vesicopustules	Similar to Case 1	Dapsone (Sulfapyridine not tried)
4. Sneddon & Wilkinson Case 4	F	53	9	Trunk, body folds, limbs	Annular, gyrate vesicles	Similar to Case 1	Dapsone and sulfapyridine
5. Sneddon & Wilkinson, Case 5	F	71	8	Neck, breasts, axillae, groin	Annular, gyrate vesicles	Similar to Case 1	Dapsone
6. Sneddon & Wilkinson, Case 6	M	68	9	Chest, groin, axillae	Pruritic, grouped vesicles	Similar to Case 1	Dapsone
7. Hellier [2]	M	54	10	Palms, soles, trunk, sides	Annular and grouped vesicles	Similar to Sneddon's & Wilkinson's cases	Sulfapyridine & Dapsone good results
8. Carney [3]	F	41	1	Trunk, axillae, neck, arms, and legs	Vesicles and vesicopustules circinate configuration	Subcorneal vesicle Cont. PMN & Few PME	No effect with sulfapiridine for 6 days
9. Cipollaro [4]	M	51	2½	Axillae, groin, cubital, trunk	Crescentic, serpiginous groups of vesicles, pruritus	Intraepidermic bullae	Sulfapyridine Promacetin Results ?
10. Burgoon et al [5]	M	44	½	Trunk, limbs, body folds	Severely pruritic grouped vesicles	Subcorneal bullae: acantholic cells	Sulfapyridine good results
11. Greenbaum & Lee [6]	F	68	4	Abdomen, back, axillae, groin	Grouped vesicles, pruritus	Subcorneal vesicle mild inflammation	Became sensitive to sulfapyridine
12. Present report, Case 1	F	75	4	Trunk, axillae, groin, arms, legs	Individual and gyrate configuration vesicles	Subcorneal vesicle, few acantholytic cells	Temporary and partial remission with sulfapyridine
13. Present report, Case 2	F	44	4	Trunk, axillae, groins, arms, legs	Grouped vesicles	Subcorneal vesicle	Excellent result with sulfapyridine
14. Present report, Case 3	F	27	8	Trunk, axillae, groin, arms, legs	Bizarre gyrate configurations	Subcorneal vesicle, tiny subepidermal blisters	Long term partial response & control with sulfapyridine

formis, there has been a striking correlation of improvement with one of these substances in preference to any of the other known antibiotic chemicals.

From consideration of the clinical and histological features of the 11 cases which have been published and the 3 which form the body of the present report, the following summary can be made:

1. The disorder is encountered primarily in females over 40 years of age.

2. It is characterized by superficial vesicopustules which form annular or gyrate plaques with irregular spreading borders.

3. The lesions are located primarily on the torso and upper parts of extremities and involve the intertriginous areas about the breasts, axillae, and groin.

4. The lesions involute to form thin superficial crusts, followed by residual hyperpigmentation without atrophy. The lesions recur in overlapping waves of healing and persist over a number of years.

5. The lesions ordinarily will not respond to the use of local and systemic antibiotics, but, in general, response is achieved following therapy with sulfapyridine or one of the sulfones.

6. The histologic features include a subcorneal vesicle, varying in size from 0.1 mm. to several millimeters in diameter, covered by a thin keratin layer with the base formed by the granular layer, containing a thin layer of frankly purulent material consisting of serum, leukocytes, and leukocytic debris, and containing an occasional acantholytic cell in the base of the blister. The rete may be normal or slightly acanthotic and show minimal edema and exocytosis. The papillary and subpapillary layers may be involved with slight edema and a very mild round-cell infiltrate. Bacteria were not seen in the skin sections.

Summary

Three new cases with clinical manifestations simulating dermatitis herpetiformis, but with subcorneal vesicles, are reported. When a total of 14 cases are reviewed, their characteristics are seen to be remarkably constant and very much like those originally reported by Sneddon and Wilkinson.[1]

8 E. Madison St.

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Subcorneal Pustular Dermatosis

Report of a Case

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In a recent paper, Sneddon and Wilkinson [1] described cases of a chronic vesiculopustular eruption which was characterized histologically by subcorneal blisters filled with polymorphonuclear leukocytes and which affected mainly middle-aged women. A case of this type was observed recently at the Detroit Receiving Hospital and is reported here so that others may recognize the disease more readily.

The cases of Sneddon and Wilkinson were felt to be distinct from dermatitis herpetiformis, although there were similarities. The pustules were sterile, had some tendency to grouping, were accompanied by moderate to severe pruritus and some hyperpigmentation. They responded fairly well to sulfapyridine and the sulfones. Cases similar clinically and histologically were reported by Hellier,[2] whose case eventuated from a pustular eruption of the palms and soles, and by Duperrat,[3] who felt that his case was not related to Duhring's disease. Other similar cases have been presented at dermatological society meetings without definite diagnosis,[4-7] although atypical dermatitis herpetiformis, chronic benign familial pemphigus of Hailey and Hailey, pemphigus foliaceus, pemphigus erythematosus, and subcorneal pustular dermatosis were suggested as diagnoses.

Submitted for publication April 21, 1958.

Supported by the Research and Development Division, Office of the Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-584.

From the Departments of Dermatology of Wayne State University and Receiving Hospital (Dr. Hermann Pinkus, Acting Chairman). Fellow in Dermatology, Wayne State University College of Medicine.

Report of Case

History.—A 63-year-old Negro woman was admitted to Detroit Receiving Hospital for treatment of a generalized pustular, scaling, pruritic eruption of five days' duration, accompanied by moderate malaise. She had experienced several similar episodes of generalized dermatitis during the 6 months prior to admission and had had three or four episodes during the 20 years since the onset of her skin disease. These acute generalized exacerbations would last 10 to 14 days and then subside to a chronic pruritic vesicular and scaling eruption of the extremities with resulting hyperpigmentation.

Past History.—The patient had been seen 13 years and 10 years previously regarding this same skin disease. A biopsy specimen was described as a large vesicle just becoming purulent, the roof of which was formed by the horny layer only. A diagnosis of dermatitis herpetiformis was made, and the patient was given sulfapyridine, to which she responded.*

Physical Examination.—Temperature, 98 F; pulse, 82; respirations, 20. The abdomen, scalp, distal parts of the extensor surfaces of the upper extremities, and most of the lower extremities were covered with very superficial, flaccid, fragile, dome-shaped bullae 0.5 to 1 cm. in diameter, filled with turbid fluid. Many of the lesions had opened, dried, and were exfoliating, but no denuded areas were present. The lesions appeared to be composed of only the most superficial parts of the skin, and the scaling which followed their drying was likewise striking in seeming to affect only the surface of the skin. Nikolsky's sign was negative. There was hyperpigmentation where previous lesions had been. There were no oral or anogenital lesions. Remainder of the physical examination was normal.

Laboratory Work.—Hemoglobin, 12.6 gm.; WBC, 7400; fil., 54%; bands cells, 8%; eosinophils, 2%; lymphocytes, 32% (a few atypical); monocytes, 4%. Urinalysis: sp. gr. 1.023, sugar 0, albumin +, WBC 3-6, RBC 0, casts and epithelium 0. Blood:

* This information was supplied by The University Hospital, University of Michigan, Department of Dermatology and Syphilology, A. C. Curtis, M. D., Professor.

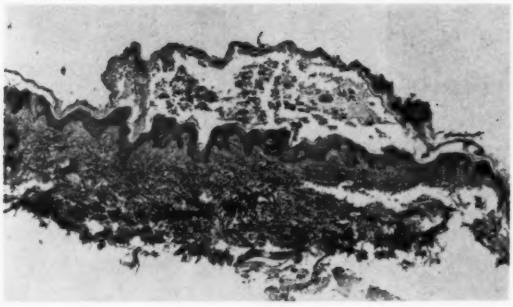

Fig. 1.—Subcorneal pustule during acute episode. Orcein-Giemsa stain; × 23.

urea N, 15 mg. %; dextrose, 124 mg. %; repeated 2 hour postprandial, 98%. Eosinophil count 427 per cubic millimeter. Blood culture: no growth. Urine culture: Micrococcus citreus, hemolytic, coagulase-negative. Chest x-ray was normal.

Histology.—A specimen was taken of a vesicle of the skin of the right arm (Fig. 1). The epidermis is somewhat acanthotic and thrown into folds. The stratum corneum is lifted off, and the space beneath it is filled with coagulated serum and leukocytes. No micro-organisms are seen. There are some leukocytes and eosinophils migrating through the epidermis, which is not particularly edematous and shows no evidence of acantholysis. There are some leukocytes in and around blood vessels in the cutis, but there is not other remarkable evidence of inflammation.

Hospital Course.—The patient improved rapidly, forming fewer and fewer pustules, on a regimen of $KMnO_4$ baths, chloramphenicol (Chloromycetin) 250 mg. q. i. d. and diphenhydramine hydrochloride, U. S. P. (Benadryl) 50 mg. q. i. d. She was discharged from the hospital after five days. Two weeks later she had a slight exacerbation which cleared without specific therapy in one week and then continued to form new lesions at irregular intervals, one or two per week. The lesions disappeared completely for several weeks while she was receiving therapy with prednisolone 5 mg. t. i. d., only to recur. Therapy with sulfapyridine 0.5 gm. t. i. d. produced a remission lasting two months.

Subsequent Course.—The vesicles, since the patient's discharge from the hospital, have been tense and acuminate, 0.5 cm. or less in diameter, filled with a turbid fluid. There has been a slight tendency to grouping on the extensor surfaces of the extremities. There is associated pruritus and hyperpigmentation but little scaling. Since the lesions had definitely changed their clinical appearance, a biopsy specimen was taken of a lesion which was felt to be a subepidermal vesicle. There was a thickened stratum corneum, separated from the rest of the epidermis by thick edema fluid containing no cells. There was again no acantholysis and remarkably little inflammatory infiltrate in the cutis (Fig. 2).

Comment

While the clinical picture of this case changed somewhat from that described by Sneddon and Wilkinson, the histology did not. The tense vesicles which were thought to be subepidermal were found to be subcorneal. The response to therapy with sulfapyridine is similar to the previously described cases. Clinically, this case and

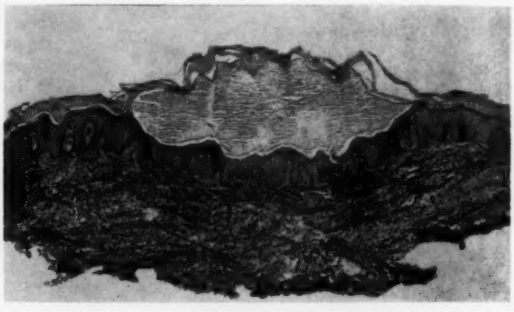

Fig. 2.—Subcorneal vesicle during chronic phase. Orcein-Giemsa stain; × 23.

one other recently observed case present very superficial vesicles and bullae filled with a turbid fluid, which proceed to superficial scaling. These lesions may or may not display grouping, often affect the extremities, but may be almost generalized. The lesions tend to recur, although response to therapy is prompt and remissions may last many months. They resolve with residual hyperpigmentation and are very pruritic. The prognosis is good; apparently the general health of the patient is not affected. Thus, clinically, subcorneal pustular dermatosis appears similar to dermatitis herpetiformis, which, by Duhring, was described [8] as having a superficial pustular form, similar to impetigo herpetiformis.

Histologically, the lesions are more difficult to classify. The bulla is like that of impetigo contagiosa, but it is sterile. The bullae of pemphigus foliaceus and of pemphigus erythematosus are superficial also, but in the cases described by Sneddon and Wilkinson, few if any acantholytic cells are found and the lesion is even more superficial. Bullae of dermatitis herpetiformis may be found within the layers of the epidermis [9] as well as subepidermally and are described as tension bullae. The same applies to the bullae of bullous pemphigoid.[10] The chronic vesicles which this case presents (Fig. 2) might be due to edema fluid and so could be related to these latter diseases. As has been emphasized,[11,12] it is not where the bulla lies, it is its structure which is the important point. It is suggested that, until more of these cases can be studied, they be considered as a separate entity under the name given by Sneddon and Wilkinson, subcorneal pustular dermatosis.

Summary

A case of subcorneal pustular dermatosis known to be of 13 years' duration is presented.

The clinical and histologic findings are discussed.

It is suggested that these cases be considered a separate entity until experience with them has been accumulated.

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Treatment of Hypertrophic Lichen Planus with Prednisolone Butylacetate

The Use of Prednisolone Butylacetate (Hydeltra-T. B. A.) in Hypertrophic Lichen Planus Utilizing the Vibra-puncture Technique

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The purposes of this clinical study are the following: (1) to demonstrate the use of the vibrapuncture technique on a different clinical entity than the one for which it was employed by the author in a previous study [1] (lichen simplex chronicus) and (2) to evaluate the results of a new steroid preparation which was employed in the vibrapuncture procedure for this series of cases.

In the previous study, hydrocortisone acetate was discussed. Among the local effects were the inhibition of anaplasia [2] of the epidermis and an anti-inflammatory effect in the cutis.

In hypertrophic lichen planus the inflammatory infiltrate is limited to the upper cutis, although not as sharply as in the non-hypertrophic form. Secondly, in the hypertrophic form of lichen planus there is a marked acanthosis, which, as has been pointed out recently, can undergo malignant degeneration.[9]

Therefore, this entity seemed particularly suited for the Dermejector technique, which would deposit the steroid preparation at the desired level in the cutis.

Previous therapy for hypertrophic lichen planus has been generally unsuccessful.

However, Meara [3] reported one patient with this variant of lichen planus who responded well to an intravenous drip of 15-25 mg. of corticotropin (ACTH) and 2000 units of heparin in 1 pt. of isotonic saline. Therapy was given intermittently for a period of four weeks.

Submitted for publication June 20, 1958.

Kristjansen and Reymann [4] used corticotropin in eight patients with hypertrophic lichen planus and found that, although the immediate response was excellent, relapses occurred promptly on withdrawal of therapy.

Domonkos [5] treated three patients with this condition, employing a 24-gauge needle (syringe and needle technique) to inject a prednisolone suspension directly into each lesion. He stated that all lesions regressed completely, although there was residual pigmentation.

I have used this technique but would not infrequently be faced with the problem of some subsequent atrophy.

Materials and Technique

Prednisolone butylacetate (Hydeltra-T. B. A.)** is a very soluble ester of prednisolone which has been found to produce a longer and more pronounced anti-inflammatory effect than hydrocortisone acetate when injected into synovial joints.

The vibrapuncture technique employed was essentially the same as that used by me in the treatment of lichen simplex chronicus except for the addition of a "with-holding dam" as shown in Figures 1A and 1B.†

This addition to the technique allowed for greater concentration of the solution in the area treated, as there was no draining away of the liquid. It was also found that less solution was needed to treat a large area.

The "Conway Dermejector" [7] powered through a motor-driven flexible shaft was again utilized in this procedure. The needles were set to a

* Prednisolone butylacetate (20 mg. per cubic centimeter) was supplied by the Merck Sharp & Dohme Research Laboratories, West Point, Pa.

† The "with-holding dam" was constructed for me by the Robbins Instrument Co., Chatham, N. J.

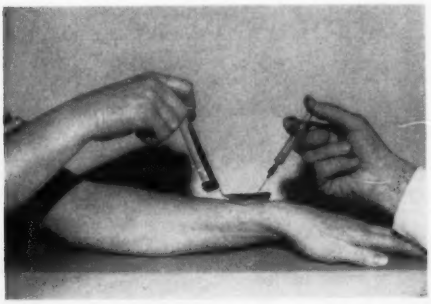

Fig. 1A.—Demonstrating the use of the "with-holding dam" while applying the suspension of prednisolone butylacetate.

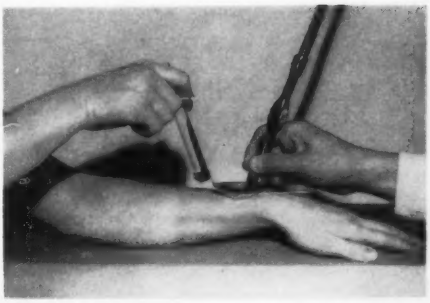

Fig. 1B.—Demonstrating the vibra-puncture technique with the "with-holding dam" still in place.

depth of 3 mm. for the first treatment because of the thickness of the plaques. Thereafter, they were set for 2 mm., as there was noticeable flattening of the lesions after the primary procedure.

The solution was dropped into the "dam" with a 23-gauge needle, after which the area was treated with the Dermejector until bleeding points were noted. Two or three drops were then added to allow for further penetration through the abraded area. During the entire procedure the "with-holding dam" was kept in place. Once the solution had been dropped into the "with-holding dam," the time required to treat a 2×2 cm. plaque amounted to less than 30 seconds. If a larger area was to be treated, the "dam" was moved along the skin; a few more drops of prednisolone butylacetate were added, and the dermejection was not interrupted.

Report of Cases

CASE 1.—A 13-year-old Puerto Rican boy had typical lesions of hypertrophic lichen planus on both pretibial regions, which had been present for five years.

Biopsy.—The epidermis showed all the characteristics of hypertrophic lichen planus, including hyperkeratosis, acanthosis, increase in the thickness of the granular-cell layer of the epidermis, basal-cell edema, and keratotic plugging of the hair follicles.

The upper dermis contained a band-like infiltrate consisting of chronic inflammatory cells and dilated blood vessels (Fig. 2).

His past therapy has consisted of bismuth sodium (Bistrimite) tablets plus various topical medications, including tar-containing ointments, antipruritic agents, and topical steroid creams.

An area on the left leg (Area 2) was selected for comparative therapy, as shown in Figure 3A. Lesion 1 was treated twice with prednisolone butylacetate with the syringe and needle technique, while Area 2 was treated twice with the vibrapuncture technique; 1 cc. of prednisolone butylacetate was instilled into each lesion.

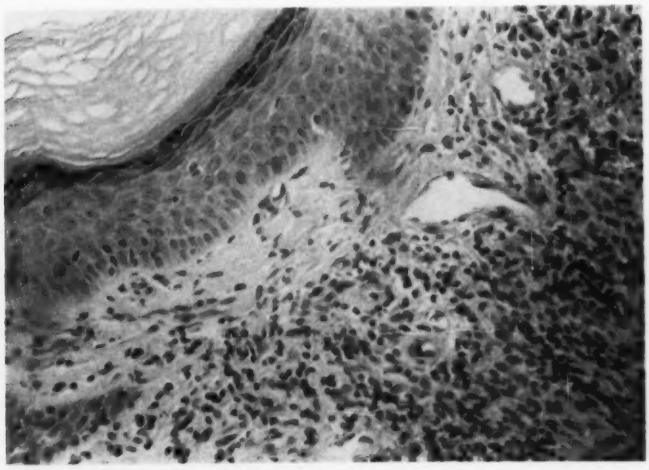

Fig. 2 (Case 1).—Photomicrograph Hypertrophic lichen planus. Reduced about 12% from mag. × 196.

Fig. 3A (Case 1).—Hypertrophic lichen planus on left pretibial region before therapy.

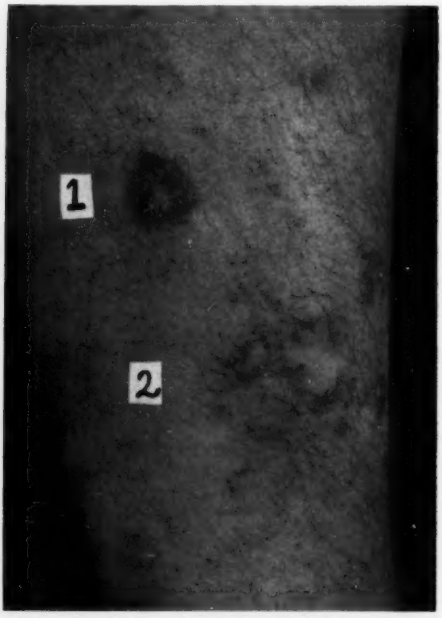

Fig. 3B (Case 1).—Left pretibial area after therapy with prednisolone butylacetate. Lesion *1*, treated by syringe and needle technique. Lesion *2*, treated with the vibrapuncture technique.

As shown in Figure 3B, there was definite flattening of the lesion treated with the Dermejector. Pruritus was relieved within 24 hours, and the lesion has not regressed for the past 6 months. Residual peripheral hyperpigmentation was noted. A noticeably smaller degree of flattening was seen in the lesion treated by the syringe and needle technique, although pruritus was relieved.

Improvement was still maintained three months after therapy.

CASE 2.—A 63-year-old white woman had a patch of lichen planopilaris (2.5×1 cm.) for 17 years in the frontal region of the scalp.

Biopsy.—The epidermis was tremendously acanthotic. The follicles were also acanthotic. The surface was slightly verrucous and covered with an increased, densely laminated, horny layer. The palisade layer was washed out. In the subepidermal region was a pronounced band-like infiltration of small round and wandering connective tissue cells. (Fig. 4).

Treatment.—Previous therapy consisted of thorium x, x-ray therapy, and various topical medications. She was treated with prednisolone butylacetate (1 cc.) by the vibrapuncture technique once a week for four weeks. After therapy there was reduction in the erythema and pruritus and a noticeable flattening of the lesion.

CASE 3.—A 12-year-old boy, with hypertrophic lichen planus in both pretibial areas of three years' duration, had received no therapy prior to his treatment with the Dermejector and prednisolone butylacetate in a similar manner as Case 1.

The patient responded well to the vibrapuncture technique, with a resultant disappearance of the pruritus and flattening of the lesions.

In none of the cases treated was a Koebner's phenomenon noted. In all cases treated with this technique, hyperpigmentation was noted. However, this was noted mainly at the periphery of each treated area.

Comment

As with the treatment of lichen simplex chronicus, the vibrapuncture technique proved to be a simple, rapid, and therapeutically successful procedure for hypertrophic lichen planus.

It was apparent that the effect of the steroid was limited to the areas treated, regardless of the quantity implanted into the dermis.

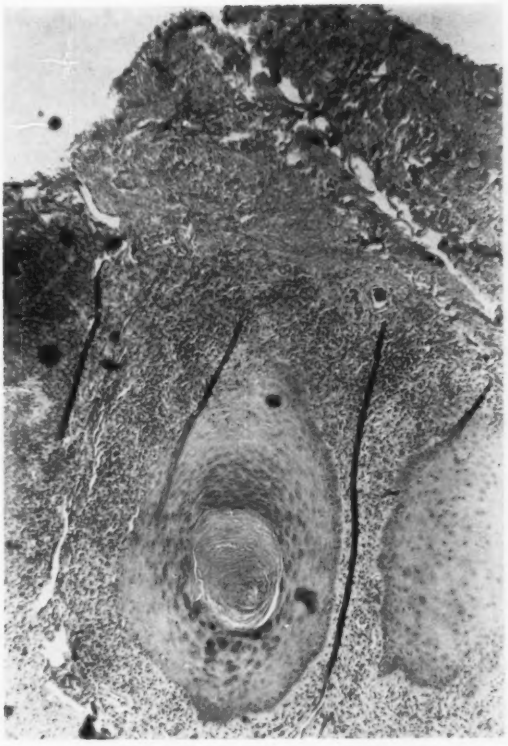

Fig. 4 (Case 2).—Photomicrograph showing typical pathology of lichen planopilaris in one portion of a plaque of hypertrophic lichen planus. Mag. × 58.

The absence of any evidence of a Koebner phenonenon resulting from the trauma of the vibrapuncture was not only gratifying but raises the provocative problem of explaining its absence.

The only possible explanation, in this group of cases, lies in the probable inhibitory effect of the prednisolone preparation.

Nardelli,[8] in a study of Koebner's phenomenon in psoriasis, came to a similar conclusion. He found the reaction to be inhibited locally by the intradermal or subcutaneous injection of cortisone or epinephrine, as well as in areas of psoriasis which were in remission.

Therefore, cortisone may well act as more than just an anti-inflammatory agent; it could possibly have an effect on the basic pathological process involved in lichen simplex chronicus, hypertrophic lichen planus, and psoriasis.

With this in mind, it stimulates one to think of the etiology of these entities as lying in the realm of either a local or a generalized enzyme imbalance or in the field of an antigen-antibody reaction, possibly of the type which is fixed to the tissues of the dermis.

Some degree of hyperpigmentation was noted in the treated areas. The etiology of this could be either one or a combination of the following factors: (*a*) postinflammatory pigmentation related to the pathology of lichen planus, (*b*) the mechanical effect of the multiple punctures produced by the vibrapuncture technique, (*c*) the local effect of the steroid suspension.

In regard to the matter of pigmentation, a similar problem presented itself when I treated areas of vitiligo with a gold suspension, employing the vibrapuncture technique. Perhaps further information will be available after a controlled series of cases

with vitiligo have been treated by the vibrapuncture technique plus a gold suspension, without the gold suspension, and with a hydrocortisone suspension.

Summary

Three patients with hypertrophic lichen planus were successfully treated with prednisolone butylacetate (Hydeltra-T. B. A.), with use of the vibrapuncture technique.

There was no residual atrophy. However, some peripheral hyperpigmentation was noted.

There was no evidence of a resultant Koebner's phenomenon.

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The Treatment of Vitiligo with Psoralen Derivatives

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During the past three years 123 patients with vitiligo have been treated with psoralen derivatives in the Dermatology Clinic, Christian Medical College Hospital, Vellore, South India. Because vitiligo is particularly disfiguring in an Indian patient, it often gives rise to severe psychological strain as well as to social stigma. In this area it is frequently confused in the public mind with leprosy, as the Tamil word for this condition is literally translated as "white leprosy."

History

Native practitioners in India have used oils of various plants in the treatment of vitiligo for centuries. An old Ayuruedic treatment consists of a purgative of figs, kine, cherry, and dill mixed with concentrated cane sugar juice. This is followed by local application of a mixture of Psoralea semina seeds (Bouchi), radish seeds, and cow's urine and exposure to sunlight up to tolerance of the patient.[1] Panja and Maplestone reported the use of Bouchi oil locally or intradermally in 1940.[2]

The work of Fahmy and Abu-Shady, in 1948, in isolating the active principles ammoidin, ammidin, and majudin from the plant Ammi majus Linn., found in the Nile valley, is well known.[3] These were found to be identical with xanthotoxin (8-methoxypsoralen), imperatorin (8-isoamyleneoxypsoralen), and bergapten (5-methoxypsoralen), respectively. The last is the main component of bergamot oil, which was used successfully in conjunction with phototherapy for the treatment of vitiligo by Cohen, in 1933.[4] Dr. Mukergee, of the Central Drug Institute, Lucknow, India, reports that these compounds are also present in Bouchi oil, which was being used by our department with varying results before purified preparations were available.[5] Carvalho advocates local use of croton oil with ultraviolet light in vitiligo.[6] Cochrane describes the pigmenting effect of hydnocarpus oil (chalmougra oil) in hypopigmented lesions of leprosy.[7] An analysis of these oils would be interesting and informative.

Although methods of administration differ widely, numerous investigators in recent years have reported encouraging results with psoralen derivatives in clinical trials in Egypt, in the United States, in France, and in India.

Drugs

Drugs used in this series of cases are as follows: Meladinine (Grimault) tablets, containing 10 mg. 8-methoxypsoralen plus 5 mg. 8-isoamyleneoxypsoralen; Oxsoralen (Paul B. Elder Company) tablets, containing 10 mg. 8-methoxypsoralen only, and Meladinine solution, containing 7.5 mg. 8-methoxypsoralen and 2.5 mg. 8-isoamyleneoxypsoralen per cubic centimeter alcoholic solution. One case used Bouchi oil (Psoralia corylifolia Linn.; family, leguminosae) locally, and two cases were given Ludermol, a sterilized preparation of Bouchi oil for intradermal injection into the lesion.

Program of Treatment

Ninety-four patients received oral medication only (Meladinine, eighty-five cases; Oxsoralen, two cases; Meladinine and Oxsoralen at different times, seven cases).

Submitted for publication Feb. 7, 1958.

Department of Dermatology, Christian Medical College Hospital, Vellore, South India.

Presented at the meeting of the Indian Medical Association, Chittoor Branch, Feb. 15, 1958, at Punganur, Chittoor District, South India.

This variation was due primarily to import restrictions and difficulty in obtaining the drugs. Starting dosage was 2 tablets daily after breakfast followed two hours later by exposure to sunlight for 10 minutes; exposure time was increased gradually to a total of 1 hour of exposure daily. Some patients who were exposed for two hours did not seem to show any additional benefit. If blistering occurred, medication was stopped for several days and restarted with a 10-minute exposure time. If patients did not respond within two or three months, they were asked to increase the dosage to 3 or 4 tablets daily in a single dose. Unfortunately, most of our patients could not afford this and remained at a minimum dosage level. Children were given 1 tablet daily; this dosage was increased in three cases to 2 tablets, without symptoms, and in one case the increased dosage caused anorexia.

Ten patients received local medication only. The solution was applied in the clinic two or three times weekly, and patients were instructed to expose lesions to sunlight after a two-hour interval for a period of 1 minute, increasing exposure gradually to a total of 15 minutes. Few patients could tolerate more than 15 minutes because of a much higher incidence of blistering and local reaction than in those patients taking oral medication. Those who could not tolerate full-strength solution were given a 50% solution diluted with alcohol.

Nineteen patients had a combination of oral and local medication either at the same time or separately. As it has become apparent that combined treatment produces better results, we are now encouraging our patients taking oral medication to come once a week for local application as well.

Most of our patients have had one or more periods of interruption of treatment for a month or longer, primarily because of lack of funds. Consequently, the duration of treatment is recorded as the total number of months during which treatment was given, rather than from the time of the patient's first visit to the clinic.

Side-Effects

As mentioned above, blistering was much more frequently found in patients with local treatment. Usually this was due to initial overexposure, and in nearly every case it was controlled by a more cautious exposure regimen.

Patients taking oral medication occasionally complained of anorexia, nausea, vomiting, irritability, or nervousness, in that order. These symptoms were more marked at the higher dosage level. In a few cases patients were able to tolerate the higher dosage only on alternate days.

One patient exhibited a mild hypertension (150/110) plus nervousness, insomnia, irritability, muscular tremors, and palpitation when taking 2 tablets daily. These symptoms disappeared twice on discontinuance of the drug. Blood pressure was normal prior to treatment, and ECG taken during height of symptoms was normal. Within five days of discontinuance of treatment, blood pressure was 130/90. With ¼ grain (0.0162 gm.) of phenobarbital taken with the drug, he was able to tolerate the drug without symptoms, but blood pressure again rose to 145/108. After his lesion was repigmented and treatment discontinued for two weeks, blood pressure was 130/92. Seven months later it was 125/88, and he has remained well.

Three of our cases with mild hypertension showed a decrease in blood pressure three or four months after treatment was started—130/95 to 95/75; 130/95 to 115/88, and 142/95 to 120/88. All other cases had normal blood pressure, and it remained normal throughout the course of treatment.

Laboratory Studies

In all patients hemoglobin, urine, and stool were examined and the appropriate treatment given for anemia, cystitis, or intestinal parasites. Blood pressure and blood

TABLE 1.—*Percentage Repigmentation with Oral Treatment Classified According to Size of Lesions*

	I		II		III		IV		Total	
Repigmentation	No.	%	No.	%	No.	%	No.	%	No.	%
0-3 mo.										
None or increase	12	20	5	22	1	5	1	8	19	17
Slight (0%-24%)	10	17	10	44	7	39	8	61	35	30
Fair (25%-74%)	8	13	4	17	4	22	2	15	18	16
Good (75%-95%)	3	5	1	4	3	17	1	8	8	7
Excellent (95%-100%)	27	45	3	13	3	17	1	8	34	30
Total	60	100	23	100	18	100	13	100	114	100
3-6 mo.										
None or increase	14	25	4	16	1	7	2	14	21	18
Slight	6	11	9	33	6	40	10	72	31	28
Fair	3	5	9	33	2	13	--	--	14	13
Good	3	5	3	11	--	--	1	7	7	6
Excellent	30	54	2	7	6	40	1	7	39	35
Total	56	100	27	100	15	100	14	100	112	100
Over 6 mo.										
None or increase	--	--	3	18	--	--	10	35	13	14
Slight	7	23	2	12	6	32	1	3	16	17
Fair	6	20	5	29	6	31	1	3	18	19
Good	3	10	4	23	1	5	2	7	10	10
Excellent	14	47	3	18	6	32	15	52	38	40
Total	30	100	17	100	19	100	29	100	95	100
Total Lesions	146		67		52		56		321	

Kahn were taken on all adults. Syphilitic treatment was given when indicated before psoralen treatment was started. Liver function tests were done on all patients with a history of jaundice or prior liver disease. Repeat tests during treatment remained normal. Patients with myocardial insufficiency or diabetes were advised local treatment only.

Diet

Patients were advised a diet rich in protein and vitamin B, but the average diet probably still remained deficient in these factors. It was suggested that limes and tamarind, rich in ascorbic acid (vitamin C), should be eaten sparingly, although their use was not completely forbidden.

Results

Repigmentation usually occurred both centrally and peripherally in each lesion within three to six weeks of the start of treatment. Peripheral pigment was initially tan or intermediate in color between the vitiligo lesion and the surrounding normal skin. Central pigment appeared in the form of hyperpigmented dots, frequently in the site of hair follicles. These central dots would enlarge and coalesce until the entire lesion was repigmented. Within two or three weeks the hyperpigmentation would assume normal skin color.

In order to assess progress, photographs were taken and the largest lesion in each area of the body was measured. They were classified according to size as follows: I, small (1 in. or less in diameter); II, medium (1 to 2 in. in diameter); III, large (2 to 4 in. in diameter), and IV, extensive (over 4 in. in diameter). On each succeeding visit repigmentation was recorded as percentage of the original lesion. Naturally, 50% repigmentation of a lesion measuring 4×5 in. involves the formation of a great deal more new pigment than does the same percentage of repigmentation in a lesion measuring 1×1 in.

Table I indicates the percentage repigmentation in lesions classified according to size. The following scale was used: poor—(*a*) no improvement or lesions increased

TABLE 2.—*Percentage Repigmentation with Oral Treatment Classified According to Location of Lesions*

	Head		Lips		Trunk		Arms & Legs		Hands & Feet		Total	
Repigmentation	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
None	3	5	7	32	8	14	10	10	25	36	53	17
Slight (0%-24%)	12	17	6	27	13	20	26	26	25	36	82	25
Fair (25%-74%)	11	16	3	14	10	15	17	17	9	13	50	16
Good (75%-94%)	3	5	--	--	12	18	8	8	2	3	25	7
Excellent (95%-100%)	39	57	6	27	19	33	39	39	8	12	111	35
Total	68	100	22	100	62	100	100	100	69	100	321	100

in size or (*b*) slight (0% to 24%); moderate—(*a*) fair (25% to 74%) or (*b*) good (75% to 94%); excellent (95% to 100% repigmentation). The results were further subdivided into three groups according to the duration of oral treatment—under three months, three to six months, and over six months.

As one would expect, a higher percentage of small lesions were completely repigmented in a shorter time than of larger lesions. In those with extensive Group IV lesions, the difference between those which repigmented completely with less than six months' treatment (7%) and those which repigmented completely with over six months' treatment (52%) is highly significant.

It soon became apparent that lesions in certain parts of the body repigmented much more readily than did others. Repigmentation of lesions classified according to location may be seen in Table 2. Lesions of the head and neck responded most readily, then lesions of the arms and legs, trunk, and hands and feet, in that order (Figs. 1-4). These findings confirm the reports of other authors that lesions of the hands and feet are extremely resistant to treatment. I also found this true of depigmentation of the lips in over half the cases.

Figure 1

Fig. 1.—Extensive vitiligo of face, trunk, and extremities before treatment.

Fig. 2.—Patient in Figure 1 after 10 months of interrupted treatment. Note repigmentation of face and chest. Hands, elbows, and lips have not yet repigmented.

Figure 2

Figure 3

Fig. 3.—Patient in Figure 1 before treatment.

Figure 4

Fig. 4.—Patient in Figure 1 after 10 months of oral treatment, 2 tablets daily. Palms did not repigment. Antecubital fossae repigmented, then depigmented again several months after treatment was stopped.

TABLE 3.—*Percentage Repigmentation with Local Treatment Classified According to Location of Lesions*

	Head		Lips		Trunk		Arms & Legs		Hands & Feet		Total	
Repigmentation	No.	%	No.	%	No.	%	No.	No.	No.	%	No.	%
None	1	20	1	33	--	--	--	--	1	17	3	12
Slight	--	--	--	--	4	66	2	50	4	66	10	42
Fair	1	20	--	--	--	--	1	25	--	--	2	8
Good	1	20	2	67	1	17	1	25	--	--	5	21
Excellent	2	40	--	--	1	17	--	--	1	17	4	17
Total	5	100	3	100	6	100	4	100	6	100	24	100

TABLE 4.—*Percentage Repigmentation with Oral and Local Treatment Classified According to Location of Lesions*

	Head		Lips		Trunk		Arms & Legs		Hands & Feet		Total	
Repigmentation	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
None	--	--	4	50	--	--	--	--	1	33	5	23
Slight	--	--	1	12	--	--	--	--	--	--	1	4
Fair	--	--	--	--	1	25	2	40	1	34	4	18
Good	--	--	1	13	--	--	2	40	--	--	3	14
Excellent	2	100	2	25	3	75	1	20	1	33	9	41
Total	2	100	8	100	4	100	5	100	3	100	22	100

Results of repigmentation in lesions treated locally are found in Table 3. These included one patient who used Bouchi oil instead of Meladinine solution and two patients who were given intradermal injections of Ludermol into the lesion. Although most of these patients had small lesions, Class I or II, response to treatment was still poor.

Results of repigmentation in lesions treated both orally and locally are summarized in Table 4. In most cases patients were started with oral or local treatment and then given a combined regimen because repigmentation was slow. It is interesting to note that the only lesions in this group to give a poor response were on the lips, hands, or feet. Because lesions on the face or scalp gave a consistently good response and lesions on the lips usually gave a poor response, we separated these two categories to show variation in response. It was also noted that lesions of the lips blistered more frequently than any other lesions. Therefore, we instructed patients to cover the lips after 15 minutes' exposure to sunlight, while other lesions on the face were exposed a full hour.

In order to evaluate methods of treatment and other factors I divided the patients into three main categories according to the best response of their lesions. Excellent (95% to 100% repigmentation) presupposes cure if treatment is continued long enough. Moderate (25%-94% repigmentation) indicates a good prognosis for complete repigmentation with continued treatment. Poor (0%-24% repigmentation) may mean that the patient will not respond to psoralen treatment. It should be noted that those who had an excellent response in one part of the body did not necessarily have an excellent response in all parts of the body, but it would seem that this is due to the location of their lesions rather than their ability to respond to psoralen treatment.

Sixty-eight patients (55%) gave an excellent response, but only thirteen (10%) were completely cured of all lesions on the body. Twenty-three (19%) were classified as moderate, and thirty-two (26%), as poor.

TABLE 5.—*Response of Patients to Various Types of Treatment*

Treatment	Excellent		Moderate		Poor		Total	
	No.	%	No.	%	No.	%	No.	%
Under 3 mo.								
Combined	4	80	1	20	--	--	5	100
Oral	13	35	10	27	14	38	37	100
Local	1	25	2	50	1	25	4	100
Total	18	40	13	28	15	32	46	100
3-6 mo.								
Combined	6	75	1	13	1	13	8	100
Oral	20	62	4	13	8	25	32	100
Local	--	--	--	--	4	100	4	100
Total	26	59	5	11	13	30	44	100
Over 6 mo.*								
Combined	4	67	2	33	--	--	6	100
Oral	19	76	2	8	4	16	25	100
Local	1	50	1	50	--	--	2	100
Total	24	73	5	15	4	12	33	100
All Patients								
Combined	14	74	4	21	1	5	19	100
Oral	52	55	16	17	26	28	94	100
Local	2	20	3	30	5	50	10	100
Total	68	55	23	18	32	26	123	100

* Of these, only 9 patients were treated 1 yr. or longer.

Fig. 5.—Extensive vitiligo before treatment.

Fig. 6.—Patient in Figure 6 after oral treatment, 1 tablet daily for one year.

Fig. 7.—Patient in Figure 6 before treatment.

Fig. 8.—Patient in Figure 6 after oral treatment for one year.

TABLE 6.—*Response of Patients According to Age and Sex*

	Excellent		Moderate		Poor		Total	
Classification	No.	%	No.	%	No.	%	No.	%
Men	28	50	10	18	18	32	56	100
Women	20	51	7	18	12	31	39	100
Total of Adults	48	50	17	18	30	32	95	100
Boys under 12	7	100	--	--	--	--	7	100
Girls under 12	13	62	6	29	2	9	21	100
Total of Children	20	71	6	21	2	8	28	100
Males	35	55	10	16	18	29	63	100
Females	33	55	13	22	14	23	60	100
Total	68	55	23	19	32	26	123	100

Of the last group only seven (6%) showed no formation of new pigment whatsoever. From this we can see that there was evidence of some new pigment formation in response to psoralen therapy in 94% of the cases.

Table 5 summarizes the response of patients to different methods of treatment. The best results were found with those patients given a combined simultaneous oral and local treatment regimen, although the number of patients treated in this way is small. Oral treatment alone gave satisfactory results, but the response to local treatment alone was generally poor. It is significant that 50% of those patients treated locally are classified as poor, whereas only 28% of those given oral medication were in this category and only one person (5%) of those receiving both oral and local treatment. This patient had discontinued oral treatment after four months and changed to local because of financial difficulties. Furthermore, hers was a lesion of over 17 years' duration (Figs. 5-8).

Duration of Disease

The average duration of the disease in the group with an excellent response was 2.9 years. Average for the moderate group was 4.1 years. For the poor group it was 5.4 years, which is almost twice that in the excellent group. Therefore, we may conclude that lesions of short duration are likely to respond to treatment faster than those of long duration.

Duration of Treatment

By studying Tables 1 and 5 we can see that there is a steady increase in percentage of repigmentation in patients who have received treatment for a longer period of time. Of the 32 patients classified as poor in Table 5, only 4 (12.5%) had received treatment for the minimum duration of six months. It is doubtful whether further treatment in these four cases would be of any benefit unless they were given a combined oral and local regimen.

Age

Table 6 summarizes response to treatment according to sex and age. Response is almost equal in both males and females. However, children respond much more readily than do adults. Only 2 children out of 28 gave a poor response. One was a girl aged 9, with depigmentation of both heels for one year. The other girl, aged 10, had depigmentation of the scalp with gray hair for seven years. Even though she was treated for only two months, some of the hairs became black. She was advised to shave the scalp and is expected to repigment with better exposure. One reason for this better response in children may be due to the fact that they have had the disease for a shorter period of time. The 20

TABLE 7.—*Response of Patients According to Distribution of Lesions*

	Excellent		Moderate		Poor		Total	
Distribution	No.	%	No.	%	No.	%	No.	%
Single lesions	3	19	4	25	9	56	16	100
Multiple lesions	65	61	19	18	23	21	107	100
Total	68	55	23	19	32	26	123	100

children in the excellent group averaged a duration of 1.2 years; the 6 children classified as moderate averaged 1.4 years, and the 2 in the poor group had depigmentation for 1 and 7 years, respectively.

Distribution of Lesions

I also studied the relationship between variation in distribution of lesions and their response to treatment. One hundred seven cases (87%) had multiple lesions on the trunk or extremities, usually with bilateral distribution. Sixteen patients (13%) had single lesions. In Table 7 we see that the response to treatment in these two groups is markedly different. Of those with multiple lesions, 61% gave an excellent response and only 21% gave a poor response. On the other hand, of those with single lesions only 19% gave an excellent response and 56% gave a poor response. It was my clinical impression that most of the single lesions repigmented slightly from the margins only, without central follicular-type repigmentation. The question may be raised as to whether this difference in response to psoralen therapy may indicate a difference in etiology between the form of vitiligo occurring as a single lesion and that with multiple lesions. Multiple lesions would suggest a systemic or generalized defect in pigment formation, whereas a single lesion, regardless of the size, might be the result of a local factor. Best results were obtained when repigmentation occurred clinically both centrally and peripherally simultaneously.

Mechanism of Action

The exact mechanism of action of the psoralen compounds on melanogenesis is unknown. They are strong photosensitizing agents and act synergistically with sunlight. With both oral and local treatment only those lesions which are exposed to sunlight or ultraviolet irradiation will repigment. However, as ultraviolet-light therapy alone gives disappointing results in treatment, there is more involved than merely enhancing the response of the skin to irradiation.

Because of the local response of repigmentation in just those lesions which are treated locally, the action must be primarily within the skin itself rather than on one of the internal glands which affect pigmentation. It is remarkable that psoralens taken orally affect depigmented patches of the skin specifically.

Several investigators have reported development of new patches of depigmentation during treatment or after treatment was discontinued.[8] In our series new lesions appeared in 32 cases (26%), usually in the first few months of treatment or after treatment was discontinued for a month or more. In most cases these new lesions were small and repigmented with further treatment. However, this would indicate that the psoralens act primarily in the skin to stimulate melanogenesis but that they do not necessarily counteract the depigmenting process if the disease is in an active phase.

Conclusion and Summary

The findings in 123 patients treated with psoralen derivatives in the Dermatology Clinic, Christian Medical College Hospital, Vellore, South India, are presented. From these studies the following conclusions are reached.

1. A combined regimen of psoralen given orally and applied locally is the most effective method of treatment of vitiligo. However, oral treatment alone is more effective than local treatment alone.

2. Treatment should be continued for at least six months to one year and longer if repigmentation is steady and continuous.

3. Lesions of the head and neck respond most favorably to treatment. Lesions of the hands and feet are singularly resistant. Lesions of the lips also respond poorly.

4. Patients in whom the disease is of short duration respond more readily to treatment than do those who have had the disease for a longer period of time.

5. Children respond more readily than do adults, possibly because the duration of their disease is usually shorter.

6. Patients with multiple lesions are likelier to respond well to treatment than are patients with single lesions. Single lesions frequently repigment only from the margins, whereas repigmentation in patients with multiple lesions is usually both central and marginal.

7. The psoralen derivatives probably act synergistically with sunlight to stimulate melanogenesis. They do not necessarily counteract the primary defect causing vitiligo, as new lesions may appear during psoralen therapy.

Dr. C. Bhaktaviziam, Head of the Department of Dermatology, Venereology and Leprosy, gave advice and cooperation in this study.

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Incontinentia Pigmenti

Report of a Family

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Incontinentia pigmenti usually begins in early childhood as a series of linear and grouped vesicles on an erythematous base, which, when ruptured, tend to become impetiginized. These may disappear and recur for weeks or months, gradually giving way to an intermediate temporary stage of linear verrucous lesions, or the vesicles may lead directly to the third or pigment stage, characterized by a reticulated pattern of pigmented macules, whorls, lines, and patches. Many years later, in some patients, a final stage may occur in which the lesions fade, leaving either no blemishes or slightly atrophic, slightly depigmented areas to mark the sites. Many cases are associated with mild to severe ectodermal and mesodermal defects.[2,3,6,11]

Since the literature, pathogenesis, and characteristics of the disease have been surveyed in detail by previous papers on the subject,[2,5,6,9,11] only some of the more pertinent cases will be reviewed here.

Under the diagnosis of systematized nevus, the first two cases (identical twins) were presented by Bardach[1] in 1925. Two years later Naegeli[7] reported three cases under the name of chromatophore nevus; the lesions were found in a father and his two daughters. A third sibling was diagnosed as having hydroa vacciniforme.

In 1938 Sulzberger[11] reported a typical case in a 19-year-old woman whose family presented three generations of developmental defects in the female members *only*. A family tree was included, and attention was focused on the familial and hereditary aspects of the disease. Only one member had skin lesions.

Two cases, a father and a daughter, both with typical skin lesions, were described by Sobel[10] in 1948. This was the first report since Naegeli's[7] cases in which cutaneous lesions appeared in more than one generation.

In 1952 Findlay[4] reported a typical case in a young girl whose mother had "a band of reticular pigmentation over the right shoulder and right side of the neck coming over the middle of the clavicle to the sternum, diagnosed as systematized ephelis." A maternal aunt had similar freckles. This constituted the third report of cutaneous lesions in more than one generation and the first report of a mother-daughter relationship.

Finally, in 1955, Philpott, Woodburne, and Philpott[8] described four cases, two pairs each of mother and daughter, with typical lesions.

The purpose of this paper is to present the case histories of what we believe to be a family with typical skin lesions in the female members for three generations.

Reports of Family Members *

CASE 1A.—J. S. T., 54-year-old man, no known lesions. He was not available for examination. History from G. M. T.

CASE 1B.—G. M. T., 42-year-old woman. She gave a vague history of skin lesions in infancy. Unfortunately, her parents are dead, and hospital records do not extend back into her childhood. At present she has two small, irregular, reticulated,

Submitted for publication March 17, 1958.

From the Department of Dermato-Syphilology, Indianapolis General Hospital (Dr. John Eric Dalton, Chairman).

* Numbers refer to the generation, and letters, to the members of each generation.

pigmented, 2×2 cm. macules on the left lower back.

CASE 2A.—J. L. T., aged 24, daughter of G. M. T. She was first seen at the Indianapolis General Hospital Pediatrics Clinic in December, 1934, with a complaint of "broken out." At that time she was 11 months old and had presented a history of vesicles and verrucous lesions for some time. Subsequently the lesions disappeared, only to be replaced by reticulated hyperpigmented lesions on both sides of her body. At present she resides in Michigan and is not available for reexamination. History is from Indianapolis General Hospital records.

CASE 2B.—E. T., aged 21, son. No lesions reported.

CASE 2C.—C. T., aged 19, son. No lesions reported. Subjects 2B and 2C are in the armed forces and are not available for examination. History is from G. M. T.

CASE 2D.—M. T., aged 14, son. There is no history of vesicles or verrucous lesions, but he presents two lightly pigmented macules on the left chest. The patient has had Jacksonian seizures since birth and a right rotoscoliosis.

CASE 2E.—D. T., aged 8, daughter. The patient was born at home in January, 1950, after uneventful gestation and delivery. The child appeared normal until the fourth day, when the mother noted numerous vesicles on the arms, trunk, and legs. Seen by the Indianapolis General Hospital Pediatric Clinic, she was treated with penicillin ointment for six to eight weeks, whereupon the vesicles subsided, leaving diffuse pigmented lesions. She was first seen by the Dermatology Clinic in April, 1950, at which time she presented slightly raised, hyperpigmented, linear and reticuliform lesions of the arms, legs, chest, and abdomen. She also had flat slate-gray lesions on the back. Histopathological sections showed only several foci of heavily laden melanophores in the upper corium and papillae. She was presented to several authorities at a special clinic in May, 1950, and a diagnosis of "linear generalized nevus" was made. After the discovery of incontinentia pigmenti in two other members (Cases 2F and 3A) of her family, the patient was reexamined in the Dermatology Clinic in March, 1957. At this time she presented reticulated, lightly pigmented, and atrophic lesions across both shoulders and descending down onto

Fig. 1.—Case 2E.

her arms (Fig. 1). Her mother states that these lesions have been steadily fading since the age of 2. No developmental defects have been found. Following review of the 1950 biopsy specimen, a diagnosis of incontinentia pigmenti was made.

CASE 2F.—M. E. T., aged 17, daughter. The patient was first seen by the dermatology department on Nov. 15, 1956, four days after the delivery of her first child. The department was asked to see the neonate because of vesicular and crusted lesions on the back and extremities. In the course of examining the infant, the mother was also examined, revealing pigmented lesions which had been present all of her life.

The patient was born on May 15, 1940. On the following day redness of the skin was noted, and on May 17 a vesicle was found on the left leg and another on the right arm. By the following day, the patient had a generalized vesicular eruption, except for the scalp, palms, and soles. The lesions were described as "small, superficial vesicles, which form in groups and close together, many of which are confluent. These vesicles frequently occur in linear groups, especially on the extremities." Impressions were bullous impetigo and generalized dermatophytosis. After local therapy with aluminum acetate solution (Burrow's solution) and thimerosal (Merthiolate) tincture, many of the vesicles cleared or dried up "leaving pigmented areas." There was no real improvement, however, and the vesicles continued to appear. Finally, since the patient was afebrile and steadily gaining weight, in spite of the cutaneous lesions, she was discharged to the pediatric clinic in August, 1940. Readmitted one week later, she was treated with 1% methylrosaniline chloride (gentian violet) for two weeks, without improvement, and was again discharged unchanged. In May, 1941, the patient was admitted for marasmus and measles. Though the hospital record does not mention a vesicular eruption, it was noted that "there are elevated, indurated areas of skin over the chest which appear to be keloids of rather massive extent." The patient did not return to Indianapolis General Hospital again until the birth of her first child. She has no recollection of any type of rash except the present one, which consists of a reticulated brown patch of pigment on the left side of her trunk, extending from axilla to hip (Fig. 2). Several small irregular patches dot both hips; these are clinically identical with the two macules found on her mother (Case 1B). Examination was otherwise negative.

CASE 3A.—D. D. T., aged 15 months, granddaughter of G. M. T. (Case 1B). The department first saw this patient on the fourth day of her life because of bullous and crusted lesions on the body since birth. Newer lesions on the abdomen and extremities were vesicular and on a slightly erythematous base. Crusted lesions were present on all parts of the body, and on the flanks, arms, and legs were linear and reticulated pigmented lesions. A clinical diagnosis of incontinentia pigmenti was made. An antibiotic

Fig. 2.—Case 2F.

Fig. 3.—Case 3A.

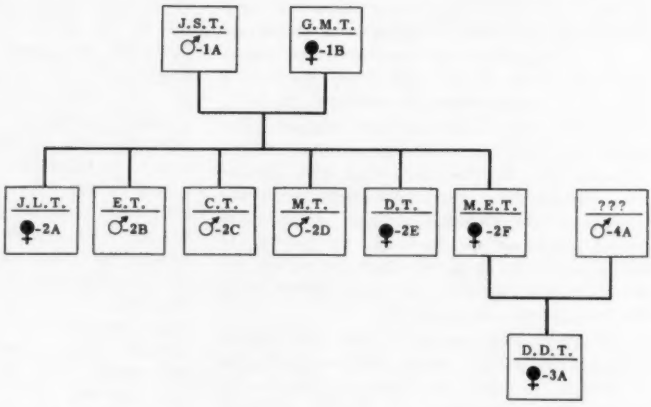

Fig. 4.—Family tree. The numbers and letters refer to the case reports. The filled-in symbols indicate the family members with skin lesions of incontinentia pigmenti.

ointment was used to control superficial infection. When reexamined six weeks later, the infant presented reticulated, hyperpigmented lesions coursing in a linear arrangement on all four extremities (Fig. 3). A few vesicles were present at the wrists and knees, and minimal reticular pigmentation could be found in the flanks. Biopsy of a vesicle showed dermoepidermal junction separation, with an eosinophilic and polymorphonuclear leukocytic band-like infiltrate beneath. Interspersed in the infiltrate were several melanin-laden macrophages. In addition, extracellular melanin was scattered throughout the area, and there appeared to be a partial loss of pigment in the basilar layer of the involved site. Two weeks later, all lesions seemed to be fading, and by the time the child was 3 months of age no vesicular or verrucous lesions were found, but reticular pigmentation persisted on the trunk and extremities. The skin was otherwise smooth and soft. X-ray survey indicated that the spine, long bones, and jaw were normal. Dentition and growth of the child have been normal, and by the age of one year the leg lesions had become lighter in color, depressed, and somewhat atrophic in appearance.

CASE 4A.—Father of D. D. T. (Case 3A). Nothing is known about this person.

Summary and Comment

Incontinentia pigmenti is briefly described, and the literature pertaining to the cutaneous lesions in more than one generation is briefly reviewed.

A family tree is herein reported in which all the female members for three generations displayed the cutaneous lesions of incontinentia pigmenti. These cases tend to support the sex-limited mode of inheritance.

One male member of the second generation presented developmental defects without skin lesions. Since no defects were found or reported in any other members, it remains conjecture whether these defects are associated with incontinentia pigmenti or are mere coincidence.

The fourth stage of incontinentia pigmenti, that in which the lesions fade and perhaps disappear, is frequently overlooked. Two of the cases in this paper (Cases 2E and 3A) are at present in this stage, and two other patients (Cases 1B and 2F) have passed through this stage and their conditions have stabilized with minimal pigmentation. This fourth stage makes the acquisition of detailed family histories difficult, as patients tend to forget "skin blemishes" of their childhood.

This family tree points out the need for accurate description of skin lesions in hospital and clinic records. This entire family history was uncovered by backtracking after the birth of Patient 3A.

Dr. George H. Mitchell aided in the preparation of this paper.

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"Chrome" Dermatitis

A Study of the Chemistry of Shoe Leather with Particular Reference to Basic Chromic Sulfate

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Dermatitis from shoes may be a most disabling type of eruption, especially if the cause is not recognized. Treatment for such eruptions of the feet, when the cause is not removed, is not successful. The physician is usually able, after appropriate study and experimentation, to pinpoint the cause, remove it, and then clear the eruption. Dermatoses of the feet have been proved to be due to dyes or other chemicals in the leather,[1,2] to the thermoplastic material used in the box toes of shoes,[3] to rubber adhesives in shoes,[4] and to the myriad other substances that go into the leather.[5-9]

In his attempt to elicit the cause of an eruption of the feet, however, the physician has been guided for years by certain accepted dicta: first, that the chromium which is used in tanning most hides into shoe leather cannot cause such eruptions, inasmuch as it is not "hexavalent," and "only 'hexavalent' chromium can cause skin disease"; and, secondly, that this chromium is firmly fixed in the leather and cannot easily be removed. It is the purpose of this article to point out that both of these long-taught "principles" are incorrect, and that, therefore, if a person sensitive to certain chromic salts is afflicted with recurrent "shoe leather dermatitis," the cause may well be the chromium in his shoes, leached out and deposited on the skin by human perspiration. During the past year, my research into this subject, as presented herewith, has demonstrated that the "hexavalent" theory is entirely unfounded. The leather chemists[10] have recently established that the perspiration of certain people can solubilize the chrome of their shoes and cause it to migrate within the fibers of the leather.

Dermatologists seeking to ascertain whether the chromium in leather was the cause of eruptions have not hitherto had available for patch-testing purposes any of the chromium compounds that will tan leather. The tanning industry deposits a basic chromic sulfate in the hide fibers and fibriles. In the conversion of the hide into leather, a representative compound of this type would be the one-third basic chrome sulfate. $[Cr(H_2O)_5OH]SO_4$, which is now available to the medical profession. This is a report of the use of this specific chemical in patch tests, along with a discussion of its chemistry, the chemistry of leather manufacture, and an exposition of Werner's theory of secondary valences[11] as it pertains thereto.

Manufacture of Leather

(*a*) *Pre-Beam-House* Processing.*—The skins are first received, trimmed, and sorted. Most are domestic skins, but some are imported (goatskins, kangaroo skins, etc.). The domestic hides are cured by salting, and in this state can be kept refrigerated for a period of up to five years without appreciable damage. Foreign skins may harbor anthrax and foot-and-mouth disease, and they must be disinfected by a 24-hour-soaking in a very dilute solution of sodium acid fluoride.

Submitted for publication March 1, 1956.

Read at the annual meeting of the American Academy of Dermatology and Syphilology, Chicago, Dec. 10, 1957.

* The beam house is that part of the tannery where the green hides are hydrated, dehaired, and bated.

The skins are soaked in water, which rehydrates the skin, removes soluble protein, extracts the curing salt, and tends to clean the skin. Sometimes disinfectants are added to this water soak to minimize bacterial action which would cause deterioration of the hides. Such chemicals as Santobrites, Dowicides, and ethylene diaminetetraacetic acid are used as disinfectants. Workers may develop sensitization dematitis from these disinfectants.

(*b*) *Beam House Processing.*—After the skins are soaked and softened, the next step is the removal of the hair so that the hide may be processed properly. The hairs are loosened by soaking the hides in lime—this being known as "liming." The alkalis used are calcium hydroxide and sodium sulfide. The alkaline sulfide solutions reduce cystine to cysteine, destroying the epidermis and loosening the hairs. The alkalis also cause swelling of the skins. After the hairs are softened, the skins are dehaired and defleshed by machine and washed in water. Workers engaging in liming and in the defleshing may develop lime dermatitis, lime ulcers, and lime eye burns.

The hides are next "bated," that is, they are soaked in a solution of salts and pancreatic enzymes. The salts used are ammonium chloride or ammonium sulfate. The bating solution completes removal of the epidermal debris, dissolves some of the elastin, cleans the grain, and neutralizes the alkalinity caused by the liming solution. At the end of the bating process, the hides are acidified with sulfuric acid. These acids and salts may cause eczematized dermatitis, skin ulcers, or nail changes.

(*c*) *Tanning Hides.*—Now the hides are "pickled" in paddle pits or large drums, in a solution of acids and salts. Varied amounts of sodium chloride and sulfuric acid are used. The acid causes further deliming of the skins, and the salt suppresses the swelling from the acid which would otherwise occur. All leather which is to be chrome tanned must first be pickled, as the pickling places the hides in an acid condition which enables them to receive the chromium. Since the pickling also acts as a temporary preservative, stock in this condition can be held for long periods of time.[12] Sensitization dermatitis to the acids and salts may occur in workers engaged in pickling.

Tanning the hide gives it increased chemical and biological stability in comparison to the original skin. Tanning reduces the sensitivity of the skin to water and putrefaction.[13] Chrome tannages are used especially for light, flexible leather such as shoe-upper leather, garment leather, etc. Vegetable tannages are used primarily for heavy leathers, such as sole leather, belting leather, etc. In this paper, I shall confine the scope to chrome tanning.

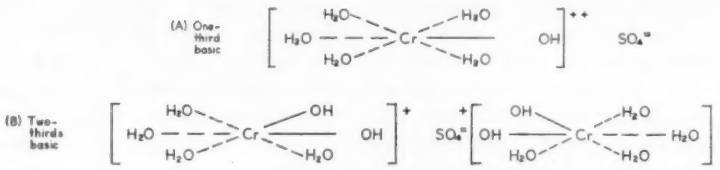
Chrome Tanning

Chrome tanning is accomplished by the use of basic trivalent chromic coordination salts. Only complex basic chromic salts have tanning power. A basic chromic compound is one which contains one or more hydroxyl radicals (OH^-), complexly bound. Though the chromium kernel of the complex compound is trivalent, the chromium complex may vary in charge from 3^+ through 0 to 3^- as a result of the penetration of hydroxyl and other negatively charged ligands into the complex. Such chromium complexes may thus possess either anionic, nonionic, or cationic properties, dependent upon the charge of the complex. Thus, the chrome used in leather tanning shows several valences:

Oxidative 3^+.

The valence of the radical is 3^+ to 3^-.

Leather may be chrome-tanned in either the one-bath method or the two-bath method. In the one-bath method, the tanning solution is prepared by reducing sodium dichromate with glucose in the presence of sulfuric acid. Complex coordination compounds are formed, the most important being the basic chromic sulfates, with the formulas:



The glucose breaks down into complexes "such as organic acids whose anions can displace some of the water radicals of the basic chromium compounds, and these more complex salts give a plumper, fuller leather." [12] Sulfur dioxide may also be used as a reducing agent, but the leather does not have the plumpness of "feel" of leathers made with sugar-reduced liquors unless the properties of the tanning liquor are modified by adding agents such as salts of organic acids to the liquor. These agents are known as "masking agents" and are also added to sugar-reduced liquors to modify the leather properties.

The chromium nucleus, then, that tans shoe leather can be extremely complex, but the only chrome tanning complexes that produce satisfactory tannages contain one or more hydroxyl groups in the complex. No other chrome compounds tan hides except these basic chromic compounds.

The hides are soaked in the chrome solution, and the chrome is fixed to the skin by neutralization with bicarbonate of soda, borax, or sodium formate.

In the two-bath method, the skins are first soaked in a solution of acidified sodium dichromate, and in a second bath the dichromate is reduced by a solution of sodium thiosulfate. This results in the formation of the above described trivalent basic chromic salts. This deposited chrome is also fixed by bicarbonate of soda or by borax neutralization. The chromic salts may cause sensitization dermatitis and ulcers of the skin or nasal septum.

The leather is then split, dyed, fatliquored, dried, finished, pressed, ironed, embossed, etc. Sensitization dermatoses may occur from fatliquored oils, or from the dyes. Fungicides are added to certain leathers during the finishing processes, and these cause a small number of sensitization dermatoses among the finishers.

Clinical Aspects of Shoe Leather Dermatitis

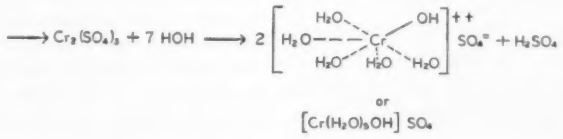
For years, dermatologists, who have had under their care patients with eruptions suspected of being caused by shoe leather, have been patch-testing with various chemicals, none of which, however, is capable of tanning hides, and none of which would be found in the shoes. Thus, in the literature, I have found that patients have been tested with ammonium or potassium dichromate (which are hexavalent), with chromium acetate or chromium chloride, chromium phosphate or chromium carbonate, or with chromium nitrate, chromium oxide or chromium fluoride. There is no report in the literature of positive tests to these chemicals when the authors were looking for shoe-leather dermatitis. However, it is a fact that none of the above chromium compounds is found in shoe leather. In the absence of such positive evidence, dermatologists have been forced to conclude that the chrome in chrome-tanned shoes was not the cause of any "shoe leather dermatoses."

While dermatitis from the chrome in shoes is rare—occurring in my practice in approximately only two patients a year—when it does occur, if it is not recognized, it is very disabling and can persist for years. J. W. Jordon and Osborne have "clinically known for years that chrome in the shoes was the cause of shoe leather dermatitis" [14] but could not prove it because they did not test with a basic trivalent chromic salt, owing to the fact that, although such was known to the leather chemists, it

was not available to the dermatologists. Leather chemists [10] have shown that the chromic salts of the shoe leathers can become soluble in perspiration and migrate within the fibers and fibrils of the shoe leather. It is my contention that such soluble salts dissolving into the perspiration would form a chemical substance which would not only migrate within the fibers of the shoe but would also migrate into the perspiration and thus come into contact with the skin. When the dye of a dress becomes soluble and migrates within the fiber of the cloth, it gets onto the skin of the wearer, and any soluble substance in a shoe which would dissolve in perspiration and migrate within the shoe fibers to my mind would likewise get onto the skin.

In order to understand why the above-mentioned trivalent chromic salts gave negative patch tests and why the basic chromic sulfates used in my practice resulted in positive patch tests, one must understand the complex nature of the chromic salts that tan leather. The chemistry of these chromic salts was published by Werner about fifty years ago.

Werner's Coordination Theory.—Werner's theory [11] is that some atoms (Cr, Ni, Co, etc.) possess both primary valences and secondary valences. By secondary valences, these atoms can build up a complex molecule which later functions as a unit in chemical processes. Thus, chromic sulfate, according to the primary valence theory, would be $Cr_2(SO_4)_3$, which hydrolyzes in water to give the following type of chrome salt in the Werner configuration:



or

$[Cr(H_2O)_5OH]\ SO_4$

Since only trivalent basic chromic compounds will tan animal skins, they must differ from other chromic compounds. Therefore, if a patient is suspected of having a rash from his shoes, one should test the patient with a basic chromic compound such as is found in shoe leather. In the past year, I have tested patients with a 0.2% trivalent basic chromic compound. To my knowledge, this is the first use of this chemical as a patch-testing agent.

Having discussed the chemistry of the chrome salts and how complex they must be before they will tan hides, and having in my practice obtained positive patch tests to such salts (which I shall report later in this paper), it is now necessary to prove that these chrome salts can be leached from the leather onto the skin.

That chrome salts can be solubilized in the leather by perspiration was attested by the 1955 study of Roddy and Lollar,[10] which describes the detannage of shoes by perspiration. They found that some people can thus detan shoes, making the leather hard, friable, and discolored. They referred to white shoes which, after wearing, became cracked and "chrome-discolored," with the leather in the damaged areas ranging in color from green to violet. A white shoe, detanned by human perspiration, which I have in my possession, shows more migration of the green chromic sulfate solution on the inside than on the outside. It is my thesis that this chrome on the inside of the shoe can get directly onto the skin by dissolving in the perspiration. Roddy and Lollar concluded that it is the lactic acid or sodium lactate in the perspiration that causes the chrome to migrate within the fibers and fibrils of the shoes. Evidence seems to indicate that the substitution of three or more lactate radicals on the internal ring of the basic chromic sulfate is sufficient to change it from a tanning agent to a nontanning agent.

Leather chemists are not completely certain how this chrome compound unites with

collagen to form leather, but it has been said [12] that "it seems most likely that some of the polar groups of the collagen penetrate the chrome complex and thus form a secondary valence bond with the tanning salt. . . . The requirement that the tanning salts contain a hydroxyl group in the complex, however, may well point to a hydrogen-bonding mechanism. . . . Secondary valence forces seem adequate to explain the binding" of the chrome salt and the collagen of the skin. If it is the secondary valence forces that are the binding forces of chrome tanning salts, then it is obvious that they must react with the skin of the animal. Is it not probable, then, that they might also react with the skin of the human to cause some dermatoses of the feet?

Inasmuch as "chrome dermatitis" is the major form of dermatitis among leather workers, and basic chromic sulfate is known to be the cause in such cases, and since we now know that this compound can be leached onto the skin from shoes by lactates in the perspiration, then it is likely that this same basic chromic sulfate will also prove to be the major cause of shoe leather dermatitis in those who wear leather.

Preparation of the Patch-Testing Solution.—O'Flaherty suggested a chemical for proper patch testing would be a chromic lactato complex containing two lactate ions per atom of trivalent chromium.[14] This may be prepared by dissolving 15 gm. of chromic sulfate (assay, 18% chromium) and 20 gm. of sodium lactate (assay, 60% sodium lactate) in 500 cc. of water. After being allowed to simmer for four hours and then to age for 10 days, this will make up a 0.5% solution with reference to chromium content. At the time of patch-testing, a small amount of this should be diluted 50% with water and applied in the usual manner.[15]

The above chemical was not available at the time of this study; therefore, the patients were tested with the 0.2% basic chromic sulfate solution heretofore described.

Further studies are being made by other dermatologists and by me in testing people with both of these chemicals.

The following cases are reported:

CASE 1.—A tannery worker who had a contact dermatitis in 1953 from "sugar-reduced tan" was patch tested in 1956 with 0.2% basic chromic sulfate, resulting in 2+ redness with vesicles, and in a new appearance of the eruption on his forearms and antecubital fossae as a result of the patch test.

CASE 2.—A tannery worker who had had "chrome dermatitis" in 1953 was patch tested in 1956 with 0.2% basic chromic sulfate, showing 4+ redness, with vesicles and bullae.

CASE 3.—A former tannery worker, who had had "chrome dermatitis" in 1934, had a recurring dermatitis of the hands and feet for 21 years as a result of wearing leather shoes. He was patch tested in 1956 with 0.2% basic chromic sulfate, resulting in 3+ redness with vesicles.

CASE 4.—A tannery worker who had had "chrome dermatitis" off and on for 20 years was patch tested in 1956 with 0.2% basic chromic sulfate, showing 3+ redness and vesicles.

CASE 5.—A graduate nurse [10,17] had had a rash on her feet for four years, the diagnosis in 1953 having been dermatitis venenata due to shoes and in 1955 dermatitis venenata of the hands from leather gloves. She was patch tested in 1956, with 0.2% basic chromic sulfate, showing a reaction of 1+ with redness, followed by a break-out of the hands with redness and vesicles within 24 hours.

Compare the above case with Case 6 as for duration of dermatitis and its recognizability when this basic chromic sulfate solution is available for patch-testing.

CASE 6.—A telephone worker had a rash on his hands of one week's duration, and denied any rash of his feet. Examination of his feet disclosed vesicular dermatitis sharply outlined to the contours of his shoes. His hands showed a vesicular eruption. A patch test with 0.2% basic chromic sulfate solution was positive. The man was told to wear canvas or rubber shoes, and his hands and feet were soaked in cold aluminum acetate (Burow's) solution every two hours that it was possible. He continued to work, lost no time, and was cured of his dermatitis in two weeks.

In the above six cases, I have reported positive patch tests to the trivalent basic chromic sulfate in dilute solution. Since this compound has only been available to physicians for less than a year, I have not had much opportunity to test many cases with it, but one case demonstrates that this

basic chromic sulfate is not related to hexavalent chromium.

CASE 7.—A Diesel engine inspector had a contact dermatitis of the legs in 1956 from the dichromate antirust fluid used in Diesel engines. He had a positive patch test to a 0.2% solution of sodium dichromate but a negative patch test to 0.2% basic chromic sulfate.

It has been my experience in these past few months that some people are sensitive to the basic chromic sulfate alone; some are positive to the dichromate alone, and others are sensitive to both.[18] Gaul [14] has recently tested 30 to 40 patients with 0.2% basic chromic sulfate, obtaining negative results in all. Twenty-four other patients have been tested with 0.2% basic chromic sulfate in my office, with negative patch tests after 48 hours. These negative tests make it evident that 0.2% basic chromic sulfate is not an irritant.

One would suspect the dye in the leather if a patient could not wear one or two specific colors but could wear other colors without harmful effect. Obtaining dyes from shoe manufacturers for patch testing, however, would not be practical. Since leather companies use up to five hundred different coloring ingredients, it would be an enormous task—in fact, practically impossible—to find which tanner made the leather and to find the specific dye that was the causative agent.

Summary and Conclusions

Chrome salts can be leached from shoe leather by the lactic acid and lactate portion of human perspiration. This chrome can thus be deposited on the skin.

The particular chromium salt involved is a trivalent basic chromic compound of complex nature: basic chromic sulfate—$[Cr(H_2O)_5OH]SO_4$. It has lately been made available to the medical profession for patch testing, as has also a chromic lactato complex containing two lactate ions per atom of trivalent chromium.

Four patients with shoe leather dermatitis are reported as having positive patch tests to 0.2% basic chromic sulfate. Two leather workers who previously had "chrome dermatitis" also had positive tests to this compound. A seventh patient had a positive test to sodium dichromate, but a negative test to basic chromic sulfate.

This is the first report of positive patch tests to a trivalent chromium compound.

The basic chromic sulfate leached by perspiration from shoes and deposited on the skin can cause sensitization dermatitis.

This is the first report in which people suspected of having shoe dermatitis have been tested with the actual chrome salt found in their shoes. Other physicians have tested people for dermatitis due to dyes and to oher chemicals, to the rubber adhesives, or to the thermoplastic materials found in shoes, but no one has previously tested people with basic chromic sulfate.

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Addendum

Since this article was submitted for publication, chemical analysis of a nurse's stockings (whose shoes had shown green chromium discoloration) has shown them to contain large quantities of trivalent chromium.

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Keratodermatitis Follicularis Decalvans

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Follicular hyperkeratosis is a feature of many diseases. Although its nature and pathogenesis have been attributed to diverse multiple and correlated factors, it still constitutes one of the most perplexing and controversial problems in dermatology. This is particularly true of those resulting in generalized cicatricial follicular atrophy with permanent alopecia. Nor is this divergence of opinion limited to the cause of the process; it includes the problem of terminology.

In the European literature, mention is made of follicular hyperkeratoses associated with cicatricial alopecia but few cases have been reported.

In the American literature, except for Graham-Little's disease (lichen planopilaris), consisting of the triad of lichen planus, acuminate follicular lesions, and alopecia, there is no mention of a condition corresponding to that described in the report which follows.

Submitted for publication March 13, 1958.

Fig. 1.—Almost complete alopecia of eyebrows and scalp with scattered follicular hyperkeratosis on the chin.

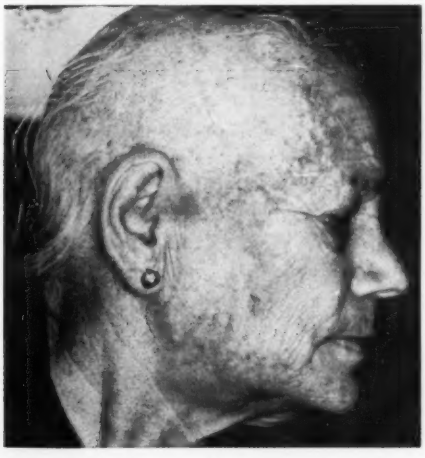

Fig. 2.—Cicatricial alopecia of the scalp. Site of biopsy is the right upper occipital area, which is surrounded by numerous follicular plugs.

Report of a Case

A 69-year-old Italian woman consulted us for the first time in November, 1949, complaining of pruritus and partial loss of scalp hair of three months' duration.

The past history was essentially negative save for poorly controlled diabetes mellitus of several years' duration.

At that time there was partial but diffuse alopecia of the scalp and the outer third of the eyebrows (Figs. 1 and 2). Hyperkeratotic follicles were present within and around the areas of alopecia in the surrounding skin. The hairs could be pulled out with ease, leaving noticeable pits. The plugs were in a patchy arrangement over the scalp and nape of the neck. No excoriations were noted.

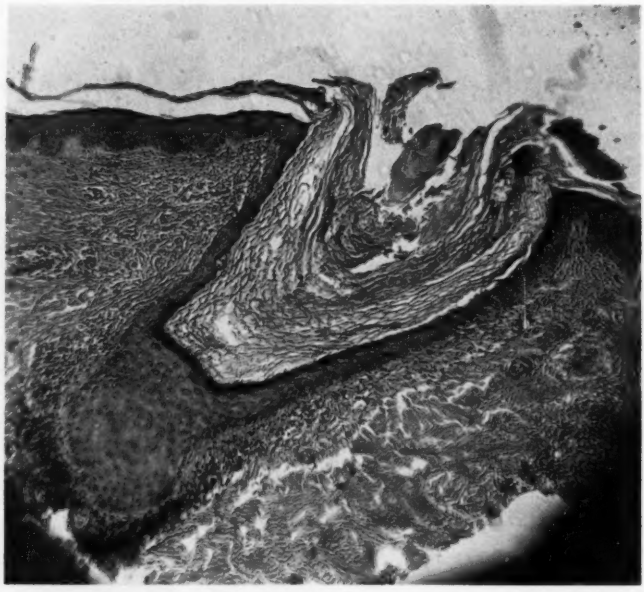

Fig. 3. — Photomicrograph of section from the shoulder. Note slight atrophy of the epidermis, which is more pronounced in the follicular lining. The follicle is dilated and filled with a lamellated horny plug.

In addition to the scalp lesions, an eruption consisting of numerous discrete, pinhead-sized, follicular, hyperkeratotic, slightly erythematous papules was present on the shoulders, external aspects of the arms, and lateral aspects of the face. At no time during the period of observation was a lichen-planus-like eruption observed. The oral mucosa was normal.

The patient received vitamin A orally and 5% ammoniated mercury ointment locally. A severe folliculitis developed. This subsided, but the hair continued to fall. By May, 1950, (5 months later) there was almost complete atrophic alopecia of the scalp and eyebrows, and by December, 1950 (15 months after the onset of the condition), alopecia of the scalp and eyebrows was complete.

A biopsy was done of the right shoulder. Following are the histological findings (Fig. 3). "The epidermis shows thinned and normal areas. At one edge is a patulous pilo-sebaceous orifice filled with keratotic plugs. In the corium, just below this is a fairly well-defined small area of perivascular infiltration of lymphocytes, histiocytes and chromatophores. The sebaceous glands show a normal structure."

Histologic examination of a specimen from the scalp gave the following findings (Fig. 4): "Almost all the follicular ostia are filled with lamellated horny material. Some of the follicular openings are appreciably enlarged showing an occasional cup shaped dilatation. In some follicles cross-sections of hair are visible, whereas several follicles are devoid of hair. The outer root sheath is edematous. Perifollicular infiltrate is sparse, and composed mainly of lymphocytes and occasionally a histiocyte. There is distinct evidence of scar tissue which is more pronounced around the hairless follicles."

Comment

It is an established fact that lichenoid, spinulous, and acneiform follicular hyperkeratoses develop during the course of infectious diseases (syphilis, yaws, tuberculosis, trichophytosis, leishmaniasis). In addition to these infectious factors, cases of lichenoid follicular hyperkeratoses also develop during vitamin A deficiency, scurvy, and occasionally in cases of frostbite and erythrocyanosis puellarum symmetrica. Follicular hyperkeratoses, therefore, are symptoms or syndromes caused by a variety of infectious agents, vitamin deficiencies, and disturbances of cutaneous circulation. It may be assumed that certain pathogenic agents at times interfere with the normal metabolism of sebaceous glands, thus causing plugging of the follicles. This assumption is based particularly on the fact that the follicular spines in scurvy and in vita-

Fig. 4. — Photomicrograph of section from the scalp. Note cup-shaped enlarged follicle filled with dense horny mass and perifollicular lymphocytic infiltration, with scarring around the hair follicles.

min A deficiency disappear readily after the administration of the respective vitamins. Diabetes was the only metabolic disorder which was clinically detectable in our patient. Disturbances of the follicular apparatus do not occur in diabetics as a rule.

Differential Diagnosis

Ulerythema ophryogenes usually involves the eyebrows, whence it spreads to the face, cheeks, upper lip, and neck. There is persistent reticular erythema with small elevated horny plugs at the mouths of the hair follicles. There are depressed scars. Alopecia of the eyebrows and other affected regions is an end-result. Superficial inflammation, with intrafollicular and interfollicular atrophy, is noted microscopically.

Folliculitis decalvans is characterized by miliary abscesses or punctiform, pinhead-sized and larger pustules involving hair follicles only of the scalp. The scalp is left dead white, thin, depressed, atrophic, and

cicatriform. Microscopically there are intrafollicular abscesses associated with perifollicular infiltrate containing a fair number of plasma cells.

Alopecia cicatrisata affects the scalp only and is characterized by thin soft atrophic shining skin suggesting "onion skin." Epidermic cones may be seen plugging follicles. Microscopically, there is no subepidermal infiltrate. There is an almost entirely lymphocytic infiltrate with a few histiocytes around the upper and middle third of follicles that spare the lower pole. The infiltrate penetrates the wall of the follicle and sebaceous gland but not the lumina of the follicles. In the late lesions the epidermis is atrophic, the corium shows fibrosis, and the follicles and sebaceous glands are absent but the sweat glands and arrectores pilorum are present.

Lichen planopilaris is associated with lichen planus lesions limited to a few areas or may be generalized. The oral mucosa is frequently involved. Histopathologically there is subepidermal infiltrate with a lymphocytic infiltrate at the lower pole of the follicle. In older lesions hair is obliterated. The follicle is dilated and filled with a keratotic plug. There is follicular arrangement of lesions of lichen planus.

Lichen pilaris usually involves the face, eyebrows, arms, forearms, legs, and thighs. On the face there are conical, occasionally obtuse papules, each pierced by a fine hair, over the brow, about the eyebrows, over the cheeks, and in the inframaxillary region. This condition is aggravated by cold weather. Microscopically there is hyperkeratosis about the orifices of the pilosebaceous follicles. The follicular orifices are widened and deepened and filled with horny plugs in which are coiled one or more hairs. There is atrophy of the root sheath, the mouth of the follicle, the sebaceous glands, and the arrectores pilorum. The hair papilla may be destroyed.

Lichen spinulosus occurs on the neck, buttocks, trochanteric regions, abdomen, thighs, popliteal spaces, and extensor aspects of arms. The face, hands, and feet are commonly spared. Clinically one sees minute papules about pilosebaceous follicles, each having a projecting horny spine. The condition is not affected by seasonal changes. The disease has its onset in childhood and never leads to atrophic alopecia.

Lichen planus follicularis circumscriptus (reported by Combes and Bluefarb [1]) consists of circumscribed discrete patches of perifollicular miliary erythematous maculopapules covered with a branny scale. There is early atrophy of the lesions without follicular plugs or punctate depressions in the atrophic areas. There is total alopecia over the involved areas.

Alopecia mucinosa, described by Hermann Pinkus,[2] is a peculiar type of follicular degeneration leading to alopecia and characterized by edema and the presence of mucin in the outer root sheath and sebaceous gland. Alopecia is not permanent.

Keratodermatitis follicularis contagiosa (Brooke-Morrow) should also be included from a differential diagnostic point of view in the group of follicular hyperkeratoses. The disease is generally of a chronic nature and affects children. While the conspicuous feature is a hyperkeratotic plug, the lesions have an acneform character. The occasional acute onset and symmetrical distribution over the dorsa of the hands, arms, and neck, gradually spreading to the trunk and lower extremities, are features distinctly different from keratodermatitis follicularis decalvans. Moreover, keratodermatitis follicularis contagiosa does not involve the scalp, and, therefore, alopecia is not associated with this disease.

There is no doubt that certain symptoms observed in our patient also occur in lichen (keratosis) pilaris. Brocq [3] divided keratosis pilaris into several forms—keratosis pilaris alba, keratosis pilaris rubra, and two intermediate divisions. In the extreme cases of the inflammatory type slight atrophy or scarring may result but is rare. According to Giovannini [4] there are atrophic changes in the sebaceous glands and atrophy of the

hair papilla. However, lichen (keratosis) pilaris has its onset in early infancy and comes to a standstill at maturity. Furthermore, complete baldness has never been observed in lichen pilaris.

Ulerythema ophryogenes has certain features in common with our case, particularly the cicatricial atrophy affecting the eyebrows and at times involving small areas of the cheeks as well as the scalp. In both diseases follicular hyperkeratosis is the predominant feature which always leads to atrophy and loss of eyebrows in ulerythema ophryogenes. At times this also occurs in lichen pilaris. Seborrheic dermatitis in conjunction with keratosis pilaris and folliculitis decalvans, according to Taenzer,[5] was the syndrome of ulerythema ophryogenes.

Our case also has some features in common with the observation of Lang[6] and Strassberg.[7] In both cases lichenoid hyperkeratotic lesions developed on the extremities which were preceded and also partly accompanied by pruritus. During the course of the disease minute pitted scars developed in the previously affected region. In both cases however, only small atrophic bald areas developed on the scalp. The disease progressed rather slowly in both instances but did not produce complete baldness. The histologic changes also resembled those found in our patient. The pathologic changes were localized and were mainly in the dilated follicles, which were filled with horny masses. In the cutis, the perifollicular infiltration consisted of round cells and eosinophilic and basophilic cells. Histologic examination of an area of the scalp showed scarring in the cutis which almost constricted the follicles. The perifollicular infiltration was similar as to the skin, but elastic fibers were not demonstrable. They designated the disease keratodermatitis follicularis atrophicans.

Furthermore, in 1915 Graham-Little[8] presented a 55-year-old patient at the Royal Society of Medicine who for 10 years had had an inflammatory process on the scalp leading to alopecia. It was accompanied by itching and keratosis spinulosa-like eruptions on the forehead, in the axillas, and on the groins. In all these areas alopecia developed. Graham-Little designated the process "folliculitis decalvans atrophicans."

A 43-year-old woman presented by Dore[9] at the June, 1915, meeting of the Royal Society of Medicine over two years developed lichen spinulosus-like lesions involving also the abdomen, back, chest, thighs, neck, and ears and leading to patchy atrophic alopecia of the scalp. There was no sign of a perifollicular inflammation.

Beatty and Spear[10] observed a woman with lichen spinulosis, first affecting the chest and finally the scalp. This patient is the only one in the literature showing association of a lichen spinulosus-like process leading to complete alopecia not only of the scalp but also of the pubic region. This occurred within a period of 10 months. The disease was identified as folliculosis decalvans.

Summary

This is the first case reported in the American literature of keratodermatitis follicularis decalvans occurring in a diabetic woman. The condition was characterized by a diffuse follicular hyperkeratosis affecting the scalp, eyebrows, lateral aspects of the face, shoulders, and external aspects of the arms. On the scalp and eyebrows the process was followed by permanent and complete cicatricial alopecia.

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Dyskeratosis Ichthyosiformis Congenita Migrans

A Variant of Congenital Ichthyosiform Erythroderma

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An interesting clinical picture characterized by slowly extending serpiginous and polycyclic lesions with raised edges, hyperkeratosis of the flexures, and hyperhidrosis of the palms, present from birth, in a woman aged 23, was first described by Comel,[1] in 1949. The back, abdomen, and proximal parts of the extremities were mainly involved; the condition became more pronounced at puberty, but there were subsequently some remissions. Comel sug-

Received for publication March 24, 1958.

From the Department of Dermatology and Syphilology, University of Belgrade (Prof. S. Ilić, M.D., Head).

Fig. 1. — Annular and polycyclic lesions of the left shoulder.

Fig. 2.—Hyperkeratosis of the left antecubital flexure.

gested the term "ichthyosis linearis circumflexa."

In a review of the literature we were able to find only one further case report under this diagnosis. Frank's [2] patient (1956), a man, showed almost identical clinical features. The condition had appeared within the first three months of life and had persisted.

We believe that the cases presented by Miescher,[3] in 1954, under the diagnosis "Kongenitale circinäre Dermatose, Typus Eczematide papulo-circinée migratrice Darier" (in a man) and by Kuske [4] as "Casus pro diagnosi" (in a girl) are essentially similar to the cases mentioned above and should be included in the same group. In the former case, the condition was present from birth, whereas Darier's case, with which Miescher compared his own, had first developed the lesions at the age of 45. In the latter case the condition had been present since infancy, although the patient's skin had been scaly and rough from her first year.

Report of a Case

A youth, aged 20, attended the outpatient clinic of the dermatological department in August, 1957, because of skin changes present from birth. He was the only child of parents who were not blood relatives, and there was no history of this or any other skin disease in the family.

His mother told him that his skin had been red and scaly at birth. Since then it had never been completely normal, although there were occasional partial remissions when only a few lesions were present. There was moderate irritation, mainly at night, but never sufficient to disturb his sleep.

Physical Examination.—On examination the patient proved to be of normal height and weight. On the trunk and the proximal parts of the extremities there were many annular lesions of various sizes with slightly raised edges. There were also polycyclic lesions formed by the confluence of several annular lesions. On the forearms and legs there were slight desquamation and lesions of the same type as on the trunk. Two flaccid bullae were seen in the left groin. In the axillae and in the popliteal and antecubital flexures the skin was hyperkeratotic and slightly brown. The palms and soles showed hyperhidrosis of moderate degree but no skin changes. The scalp was covered with greasy scales. The face was not affected. Hair, nails, eyes, teeth, and mucous membranes appeared normal.

Laboratory Findings.—Red and white blood cell counts were normal. The Wassermann reaction was negative. No abnormality was discovered in the urine. The Weltmann and thymol turbidity reactions were normal. The blood levels of potassium, calcium, and glucose were within the normal limits. The vitamin A level was 30 I. U. 100 ml.

Histopathology.—The epidermis was thickened and covered with a loose horny layer. Parakeratosis was also seen. In the papillary layer of the dermis the vessels were slightly dilated and there was an infiltrate of lymphocytes and histiocytes which was mainly perivascular in distribution. There was a mild interstitial edema throughout the dermis.

Comment

The features of our case are identical with those previously reported, with the ad-

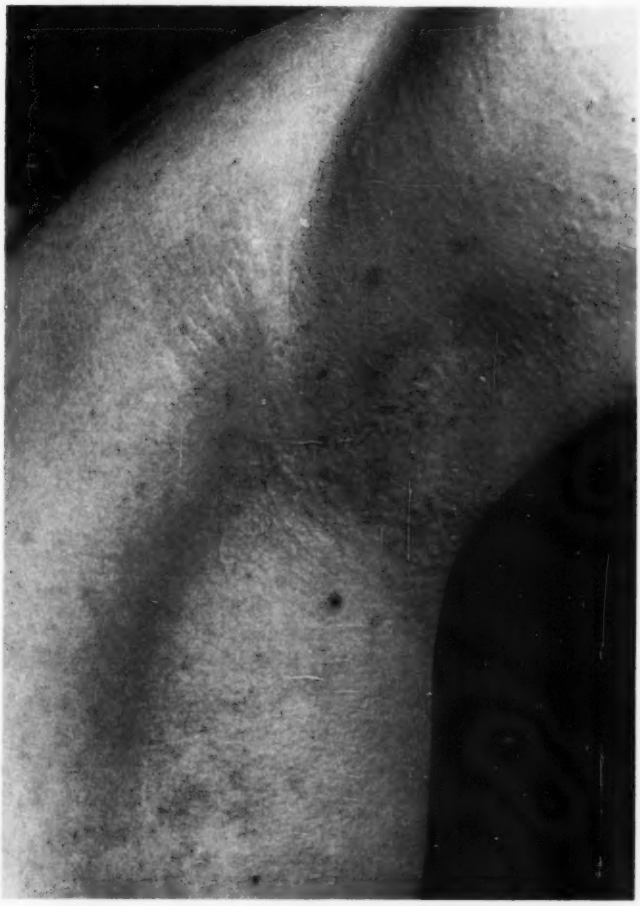

Fig. 3.—Hyperkeratosis of the left axilla (photograph taken during a remission).

dition of the occasional development of flaccid bullae.

When Comel suggested his name for this condition he considered that it resembled ichthyosis vulgaris rather than ichthyosiform erythroderma (ichthyosis congenita). Miescher postulated a special type of allergy to fungus infection with centrifugal extension and with local immunity of limited duration at the centers of former lesions.

We believe that this condition is a variant of ichthyosiform erythroderma. Both conditions are present at birth or soon after and conspicuously involve the flexures; both show pruritus, hyperhidrosis of the palms, and seborrhea of the scalp. The occasional presence of bullae in our case is a further feature which the two syndromes have in common. The histological changes in our patient are also compatible with this assumption. Hyperkeratosis of the palms and soles, often found in ichthyosiform erythroderma, has, however, not been found in this syndrome. Because of the striking configuration of the lesions and their progressive extension and the general similarity of the syndrome to ichthyosiform erythroderma, we suggest the term dyskeratosis ichthyosiformis congenita migrans." While hesitating to impose yet another term on the overburdened dermatologist, we feel that

Figure 4

Fig. 4.—Section from the left thigh. The epidermis is thickened and covered with a loose horny layer. In the dermis there is an infiltrate of lymphocytes and histiocytes, mainly perivascular in distribution. A mild interstitial edema is present throughout the dermis; hematoxylin and eosin.

Fig. 5.—Part of the same section, showing parakeratotic horny layer.

Figure 5

this distinctive syndrome requires a provisional label which is descriptive and also gives some indication of the probable affinities of the syndrome.

The cases so far reported are too few to allow one to offer a reliable opinion as to the mode of inheritance of the syndrome. It is not sex-linked, and it seems probable that it will prove to be recessive.

46a, Nemanjina St.

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A Comparative Study of Canine and Human Dermatology

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General Introduction

"A milestone in the reunion of human and veterinary medicine is, I believe, the increasing awareness of the comparative aspects of medicine." This statement, made by Dr. J. V. Klauder, keynotes our interests and endeavors in this present study.

Canine dermatology is a relatively untouched field and one which may prove informative to both disciplines. It is, therefore, our purpose to define and characterize canine dermatology and to correlate it with human dermatology, wherever possible. In so doing, new areas of investigative research for human medicine may evolve and basic information for veterinary medicine will be disseminated.

We have chosen to use human dermatology as our reference point for the following reasons:

1. Human dermatology has achieved the greater degree of advancement.
2. The language of human dermatology and pathology is more universally understood.

This work is to be presented in three parts:

1. General introduction (the subject of this presentation).
2. Comparative study of canine and human cutaneous tumors.*
3. Canine dermatoses.

Submitted for publication May 1, 1958.

Presented in part before the Symposium on Internal Medicine in Relation to Dermatology, American Academy of Dermatology, December, 1957.

Instructor in veterinary medicine, University of Minnesota; research fellow, Mark L. Morris Memorial Animal Foundation (Dr. Schwartzman). Trainee, National Cancer Institute; fellow, Division of Dermatology, University of Minnesota, Dr. F. W. Lynch, Director (Dr. Orkin).

* Supported in part by a grant from the Minnesota Division, American Cancer Society, Inc.

Veterinary research has concentrated its efforts, for the most part, in the fields of infectious diseases, bacteriology and virology, and other areas of economic importance to livestock. This is obligatory to veterinary science and has created in this country an optimum situation of animal health unrivaled in the world. Consequently, veterinary dermatology, and especially canine dermatology, has been neglected until recently when research funds have been made available and workers have become concerned about the paucity of dermatologic information. We are, therefore, at the very beginning of enlightenment and eager to disseminate information.

To facilitate an understanding or appreciation of canine dermatology, we feel obliged to give some background information. Canine dermatology represents approximately 25% of small animal cases. Some of the problems inherent in its practice are the following:

1. Rarely are good histories obtained. Few owners observe the original lesion, and, therefore, most can give little or no information concerning the initial eruption, its pathogenesis, or early course.
2. If a lesion is pruritic, only the end-result of self-inflicted trauma may be seen.
3. Careful examination is difficult, and the topography of the dermatosis is often tedious, if not impossible.
4. Economics plays an important part in client relationships. This is an obvious hindrance to the men in noninstitutional practice, who cannot utilize laboratory procedures because of the owner's unwillingness to pay for them.

Anatomy

Canine skin differs significantly from that of the human (Figs. 1 and 2). The skin is thickest on the head, neck, and dorsal and lateral surfaces of the body. Thick skin

Fig. 1.—Normal canine skin (medium lumbar back). Note thin undulating epidermis without rete pegs, numerous apocrine ducts and groups of hair follicles near the surface; × 75.

usually has a thin epidermis (less than 100μ) and a thick dermis (1000μ or more). There is no consistent pattern as to the thickness of the epidermis over thin dermal areas (26.5μ-200μ).

Normally, the epidermal surface is undulated and has minimal hyperkeratosis. In the thicker epidermis (as on the digital pads) all four layers are found, but elsewhere only the stratum germinativum and corneum are present. Prickle cells and rete pegs are absent (Fig. 3). The amount of pigment varies with the skin color. In white or light-colored areas pigment is mainly in the stratum germinativum, but in black skin it is in all layers of the epidermis.

The dermis shows no distinct separation into layers, but finer fibers characterize the superficial dermis and coarser fibers, the deeper. Mast cells are commonly found in normal sections. The hair follicles are compound and occur in groups of three to nine (Fig. 5). The sebaceous glands are generally larger in the dog than in man but are similar histologically. Apocrine glands are universal except in the digital pads (which are the only site of eccrine glands) and the muzzle (which has no sudoriferous glands).

Fig. 2.—Normal human skin (medium lumbar back); × 75.

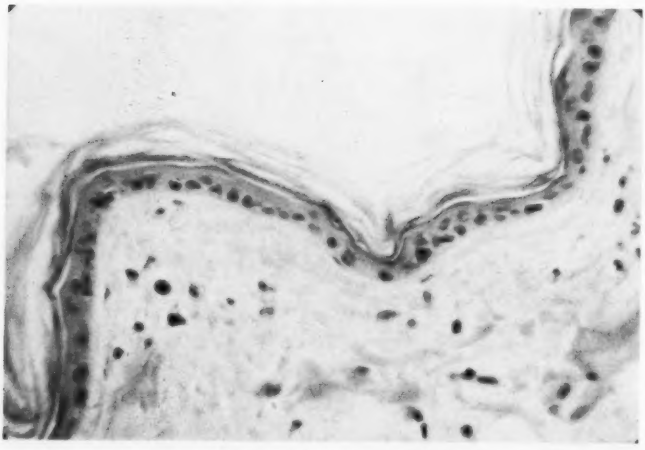


Fig. 3.—Normal canine epidermis (lateral chest). Note absence of prickles and rete pegs in thin undulating epidermis; × 330.

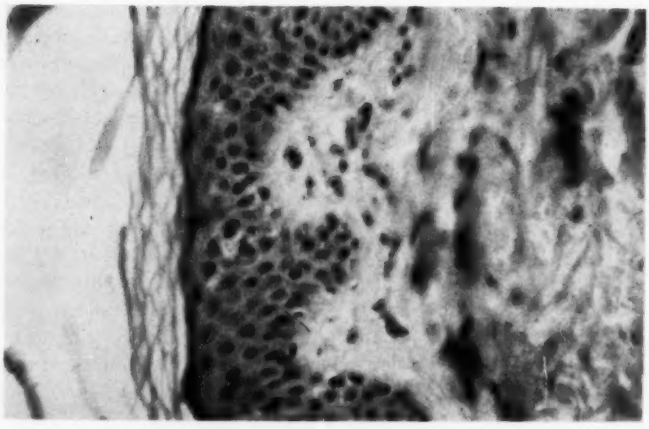


Fig. 4.—Normal human epidermis (lateral chest); × 330.

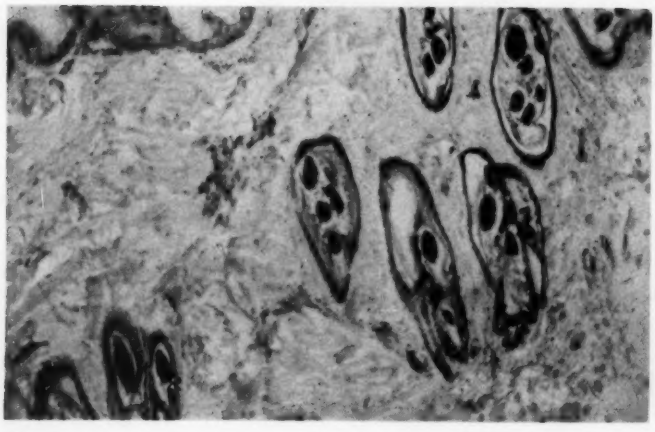


Fig. 5.—Normal canine hair follicles (dorsum of head). Note thin-walled follicles containing multiple hairs and paucity of sebaceous glands; × 75.

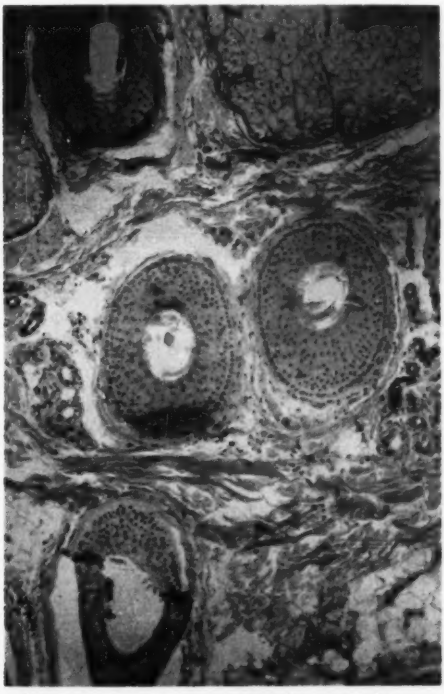


Fig. 6.—Normal human hair follicles (scalp); ×75.

Physiology

The basic physiology of the dog is well delineated, with the exception of the skin. We shall attempt, where possible, to correlate aging and hormonal processes with dermatologic entities.

The following is a guide to equivalent physiologic ages of dog and man:

Dog Age, Mo.	Man Age, Yr.
6	10
12	15
18	20
24	24

After 24 months, each canine year is equivalent to 4 human years. Thus, a 5-year-old dog would be comparable in age to a 36-year-old person, etc.

Puberty is reached between the age of 6 and 11 months. One sexual cycle in the female is approximately six months: proestrum, nine days; estrum, nine days; metaestrum, three months, and anaestrum, two months. During the estrum phase (heat) ovulation occurs. Uterine hemorrhage occurs during proestrum and estrum. The remainder of the cycle (five months) is concerned with a gradual return to normal. The dog does not go through a climacteric, though her breeding potential decreases after 6 or 7 years of age.

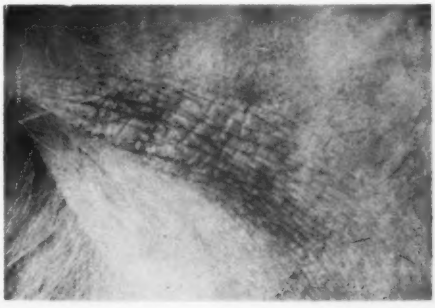
Reaction Patterns

Clinically, the canine skin has limited reactivity. Vesicles and bullae are rare. In any pruritic disease the dog must resort to rubbing, scratching, or licking to remove the cause or to replace the itching sensation. Thus, many lesions result from self-inflicted trauma, the response varying with the location. Prolonged licking of the inner thigh, abdomen, axilla, or lateral skin fold of the flank results in lichenification (macroscopically and microscopically similar to that of man) (Fig. 7). The inner surface of the pinna also shows lichenification in chronic infections. In contrast, licking of the extremities results in a fibrotic nodule or tumor, comparable to knuckle pads. Scratching, biting, and rubbing (confined to the tail base, dorsal and lateral trunk, neck, and lateral face) result in an acute, circular, purulent ulcer or in a chronic, diffuse dermatosis.

Specific Dermatoses

The only allergic reaction that we have observed in the dog is urticaria. Frequently this is seen as angioneurotic edema

Fig. 7.—Lichenification (lateral skin fold of flank).



of the face. Other allergic dermatoses that have been described bear the name only without proof. For example, seasonal pruritus, which is closely allied to human ragweed dermatitis, recurs at the same time each year (around Aug. 8) and ends abruptly with the first frost. There is associated pruritus of the feet, eyes, and nose, though the entire body may be involved. There are no evident primary lesions, and the patients have extensive excoriations. This disease is prevented or alleviated through the use of cortisone or antihistamines. We plan to apply ragweed patch and intradermal tests in these dogs and attempt desensitization.

Papular urticaria is seen in dogs infested with fleas. We have prepared a flea antigen but have failed to demonstrate hypersensitivity in these cases, probably as a result of an inadequate antigen.

Hypersensitivity to drugs is rare. We have observed only the immediate reaction to penicillin. Contact dermatitis is discussed, but there has been no scientific verification. Atopy is not commonly considered to exist in dogs. However, Prausnitz-Küstner antibodies to ascarids have been demonstrated. Atopy in dogs is worthy of further investigation.

In the area of solar dermatitis, there is an entity (common to collies, Shetland shepherds, and mixtures of these breeds) similar to the human eczematous type of polymorphic light-sensitivity. Initially, mild erythemia and alopecia appear at the junction of the hairless black part of the nose and adjacent skin. Exfoliation and crusting develop on the bridge of the nose, followed by secondary infection and ulcers. Depigmentation extends to involve the entire nose and periorbital skin. The end-result is a moist eczematous dermatitis with scaling, crusting, and bleeding. In summer the lesions are seen on the bridge of the nose and the upper lips. In winter the lesions are found on the lower margin of the upper lips, point of the chin, and along the lower mandible. This distribution is probably due to the height and angle of the sun at various seasons. The disease is relatively nonpruritic and recurs annually. The animal is otherwise normal. Sun-screening drugs (parenterally) such as aminobenzoic acid, chloroquine, and quinaerine hydrochloride (Atabrine) have given good results, as has cortisone.

Demodectic mange is common and is fatal in the rare generalized form when complicated by pyoderma. The mite, Demodectes folliculorum var. canis, creates a significant clinical entity which is something of an enigma (Fig. 8). The life cycle of the mite was unknown until recent investigations suggested that the route of infection was oral and that the organism was disseminated to the viscera as well as to the skin. Since the mite has been found in the normal skin, we are concerned about factors which bring about the changes in reactivity of the skin or the pathogenicity of the mite.

Fig. 8.—Demodectic mange. Note hair loss of lateral face and legs.

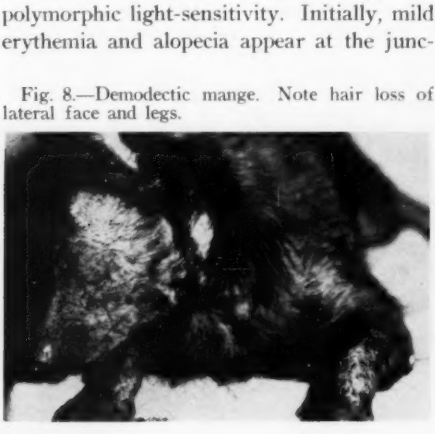
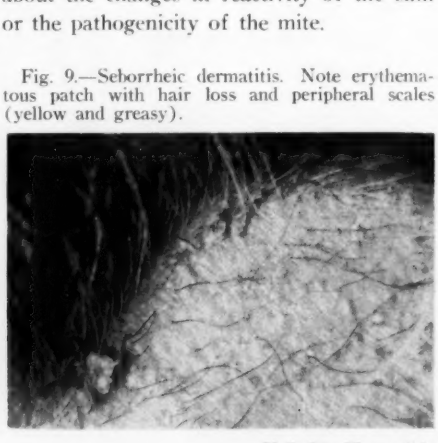


Fig. 9.—Seborrheic dermatitis. Note erythematous patch with hair loss and peripheral scales (yellow and greasy).



The seborrheic complex is commonly seen in the sicca, oleosa, and dermatitic forms (Fig. 9). The distribution is somewhat different in the dog. Common sites are the pinna (and especially the margin) of the ear, the dorsal and ventral trunk, the external thigh, and the dorsal tail.

Hormonal Dermatoses

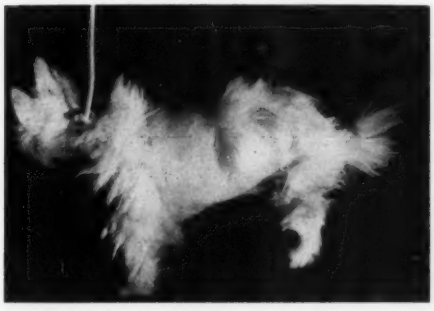
One of the most interesting groups of dermatoses is the hormonal alopecias, which are generally characterized by bilateral loss of hair without pruritus.

In female dogs shortly after spaying, and in those with irregular estrous cycles, alopecia and a squamous and crusted eruption have been observed in the groin, perianal, and perivulvar areas.

Hypothyroidism is also common. The symmetric loss of hair is diffuse but occurs mainly on the back and abdomen. The hair is dull, and the skin is thickened, rough, and scaly.

Canine Cushing's disease (caused by pituitary basophilic adenoma) has been described in dogs of middle age, with the highest incidence in Boston terriers. The onset is insidious and is characterized by roughness of hair and skin, enlargement of the abdomen, and bilateral alopecia, beginning on the legs and gradually involving the entire body. Small pustules, or blisters, develop on the abdomen and evolve to form crusts and pigmented macules. Owing to lack of antidiuretic hormone, there is diabetes insipidus.

Fig. 10.—Sertoli-cell tumor. Note hair loss at points of friction (in this case areas of contact with harness).



The Sertoli-cell tumor is usually unilateral and most often involves a cryptorchid testicle. Estrogen is secreted by the tumor, and the male dog is feminized by this secretion. This is characterized by gynecomastia, sexual attraction of other male dogs, and refinement of the skin and hair. Hair loss is seen initially in areas of friction (Fig. 10), and hair can be epilated mechanically with ease. Histologically, atrophy of the epidermis, corium, and sebaceous glands is seen.

A similar condition in both male and female dogs is seen in the age groups of 7 to 10 years. Autopsies have revealed hypogonadism in the males but no other evidence of organic disease of the endocrine glands or viscera. We consider this disease to be the result of a relative or absolute hypersecretion of estrogen by the adrenal glands. Testosterone has been the treatment of choice, but we are not yet in a position to evaluate therapy.

Deficient production of the adrenocorticotropic hormone has been reported to cause a primary disease, characterized by pruritus and diffuse or scattered hyperpigmentation on the groin.

In the area of canine endocrinology there is a need for laboratory procedures which are adaptable to the dog. The difficulty in collecting sufficient quantities of urine (for determination of steroidal hormones) and in applying indirect calorimetry (basal metabolic rate) and the absence of a procedure for the determination of progesterone present numerous obstacles. With the development of suitable techniques there should follow an understanding of the pathophysiology and thus a rational approach to therapy.

Mast-Cell Tumors

Of special interest in human and canine dermatology are mast-cell tumors. They were first reported in the dog in 1942. Numerous reports have since appeared, Scandinavian veterinarians doing most of the recent investigative work. Masto-

Fig. 11.—Mast-cell tumor.

cytomas are reported to comprise 10% of all skin tumors and 50% of those of mesenchymal origin. They are commonest in boxers and Boston terriers and are usually located in the perineal region or on the scrotum and hind legs. The tumors occur commonly between the ages of 5 and 9 years. Sex does not seem to be a significant factor. Clinically, the tumors vary considerably from pea to lemon size (the majority being about 4×3×3 cm.) and are frequently ulcerated (Fig. 11). They begin as small homogenous masses in the corium and enlarge by infiltration into the epidermis and subcutis.

Generally, mastocytomas are considered to be malignant for the following reasons:

1. The tumor grows by gradual and diffuse infiltration of surrounding tissue.

2. Lymph node involvement is frequent, and there is blockage of lymphatic and small blood vessels by tumor cells.

3. In cases where autopsies have been performed, visceral involvement is common, especially the liver and spleen.

4. Recurrence, after surgical excision, has been reported in one-third of the cases; it develops rapidly and is observed in the scar two to six months after surgery.

The canine mastocytoma is a rich source of histamine and heparin and is considered to be a site of production of hyaluronic acid. The coagulation time of blood is elevated coincidentally with the excision of the tumor, but it is otherwise normal. This elevation is probably the result of the release of heparin secondary to surgical trauma.

In Part 2 of this series (comparative tumor study) we will discuss the systemic implications of canine mastocytomas, with special reference to skeletal and hematologic findings.

Comment

In this brief discussion, multiple problems common to both disciplines are evident. A study of broad scope, as the present one, does not permit intensive investigation of every phase. It is hoped that future workers will concentrate their efforts in selected areas so that the maximum benefit to human and veterinary medicine will evolve. In those benign and malignant cutaneous condition which are analogous in the two species, the dermatologist will gain by use of the dog as an experimental animal and veterinarians will gain from the broader experience based on human dermatology.

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Local Therapy of Oral Leukoplakia with Vitamin A

DATTATREYA N. MULAY, M.D., and FREDERICK URBACH, M.D., Buffalo

That vitamin A has a marked antikeratinizing effect has been established experimentally in animals and in humans.[1] It has also been shown that this effect may be produced by topical application.[2,3] In view of reports suggesting a favorable action of vitamin A given by injection in vulvar leukoplakia[4] and senile keratoses,[5] a clinical trial of this compound in topical form seemed indicated.

Ten patients with typical oral leukoplakia of from 3 months' to 10 years' duration, ranging in severity from Grades II to IV of Thoma,[6] were treated with oral troches containing 150,000 units of vitamin A each.* The patients were instructed to remove their dentures and allow one troche to dissolve slowly in the mouth twice or three times daily. Treatment periods varied from two to six months. All patients were examined every four to six weeks, and photographs were taken for the record. In 4 of 10 patients, the diagnosis was confirmed by biopsy.

Seven of the ten patients showed very marked improvement (70% clearing or better) (Figure 1.) One patient was only slightly improved. Two patients, of whom one took the troches only intermittently, showed no improvement (Table).

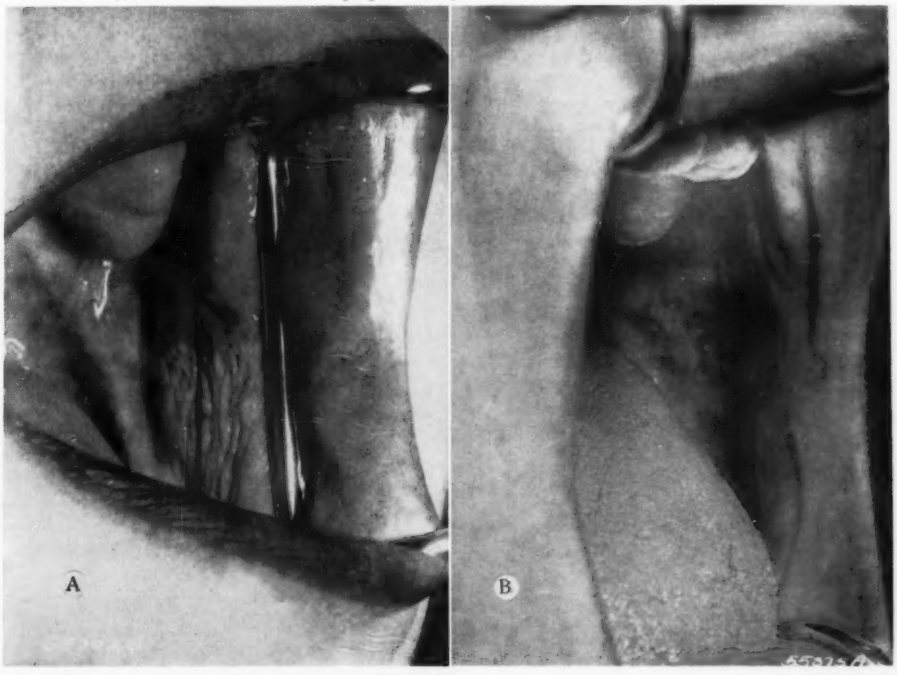
Submitted for publication March 26, 1958.

From the Department of Dermatology, Roswell Park Memorial Institute.

Supported in part by U. S. P. H. S. Grant C-2818-C. Present address, Skin and Cancer Hospital of Philadelphia, Philadelphia (Dr. Urbach).

* Dome Chemicals, Inc., supplied Vi-Dome-"A" buccal tablets, which were used in this study.

A, buccal leukoplakia prior to therapy. *B*, condition in *A* after four months of daily therapy with 150,000 units of a vitamin A preparation (Vi-Dome-"A" buccal tablets).



Detailed Breakdown of History, Symptoms, Duration of Therapy, and Results Obtained with Local Vitamin A Therapy in Oral Leukoplakia

Case	Age	Sex	Occupation	Duration of Lesion	Smoking	Area Affected	Dentures	Therapy	Duration of Therapy	Improvement, %	Biopsy
1	52	F	Domestic	4 mo.	1 pk./day	Buccal mucosa	Yes	Vit. A troches t. i. d.	3 mo.	90	Yes
2	73	M	Farmer	7 mo.	No	Lower lip	Yes	Vit. A troches t. i. d.	4½ mo.	90	No
3	48	F	Sales	4 mo.	1 pk./day	Buccal mucosa	Yes	Vit. A troches t. i. d.	8 mo.	100	No
4	47	M	Painter	1 yr.	1 pk./day	Floor of mouth	Yes	Vit. A troches t. i. d.	6 mo.	100	No
5	83	M	Clerk	3 mo.	Cigars	Lower Alveolar ridge	Yes	Vit. A troches	Irr.	None	Yes
6	51	M	Clerk	10 yr.	2 pk./day	Ant. floor of Mouth	Yes	Vit. A troches b. i. d.	3 mo.	70	Yes
7	40	M	Attendant	1 yr.	1 pk./day	Alveolar ridge	Yes	Vit. A troches b. i. d.	5½ mo.	70	No
8	58	F	Housewife	1 yr.	Occasional	Buccal mucosa	Yes	Vit. A troches t. i. d.	9 mo.	None	Yes
9	38	M	Miner	5 yr.	1 pk./day	Alveolar ridge	Yes	Vit. A troches t. i. d.	3 yr. intermit.	85	No
10	76	M	Laborer	9 mo.	Pipe	Buccal mucosa	Yes	Vit. A troches b. i. d.	6 mo.	Slight	No

It is known that a number of medicinally active compounds (cortisone, desoxycorticosterone [Doca], etc.) are absorbed easily through the mucosa, even though they poorly penetrate the intact glabrous skin. It would appear from these results that vitamin A penetrates plaques of oral leukoplakia when applied topically. It is probable that its beneficial effect is connected with interference with the pathologic keratinization which is one of the cardinal features of leukoplakia. Not enough time has elapsed to allow comment on the duration of the beneficial effect. All patients tolerated therapy well, and no toxic manifestations were observed.

Department of Health, Roswell Park Memorial Institute (3).

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Nevus Syringadenomatosus Papilliferus of the Hairy Scalp Resembling Clinically a Sebaceous Cyst

MAURICE J. COSTELLO, M.D., and MARVIN DANNENBERG, M.D., New York

Nevus syringadenomatosus papilliferus is a rare cutaneous disease which usually presents a group of firm, rose-red, millet- to hempseed-sized papules. Some of the papules may be umbilicated, resembling molluscum contagiosum. A vesicle-like component containing clear fluid is not uncommon. Stokes'[1] patient presented extensive vegetative plaques. Helwig and Hackney[2] studied 100 cases, and in all instances the lesions appeared as a solitary verrucoid patch rather than a single tumor, as seen in our patient. Sachs and Lewis[3] reported five cases, one of which had the clinical appearance of a sebaceous cyst on the upper lip. The histopathology in their case was interesting in that the predominant process was that of a mixed tumor containing cartilage and bone, while the nevoid process was deep. The heterogenous mixture of tissues would suggest teratoma. In all instances of this type of nevus the histopathologic picture is distinctive.

Report of a Case

A patient who presented a single, subcutaneous tumor with the appearance of a sebaceous cyst is reported.

A 44-year-old white man presented a marble-sized, dome-shaped, moderately firm tumor of many years' duration in the suboccipital region of the scalp. The lesion was attached to the surrounding tissues. The overlying skin of the scalp was normal, without any loss of hair. A sharply circumscribed, lobulated, half-dime sized tumor lying in the subcutis and adherent to the surrounding tissue by numerous web-like adhesions was excised with some difficulty because of this. When the tumor was divided by the scalpel after removal, a pale yellow, oily fluid was discharged.

Submitted for publication June 17, 1958.

Histopathology

Throughout most of the cutis are numerous duct-like structures which are lined by regular epithelium. The lining, for the most part, is two layers in thickness, composed of cuboidal-shaped cells, although in some areas the cells are columnar and have clear cytoplasm. In some areas the lining can be seen projecting into the lumen of these cavities. While the ducts are relatively small, some are decidedly dilated and cystic. The surrounding cutis shows a mild reaction composed of small round and wandering connective tissue cells and decided fibrosis. There are also dilated blood vessels, many of which contain blood elements.

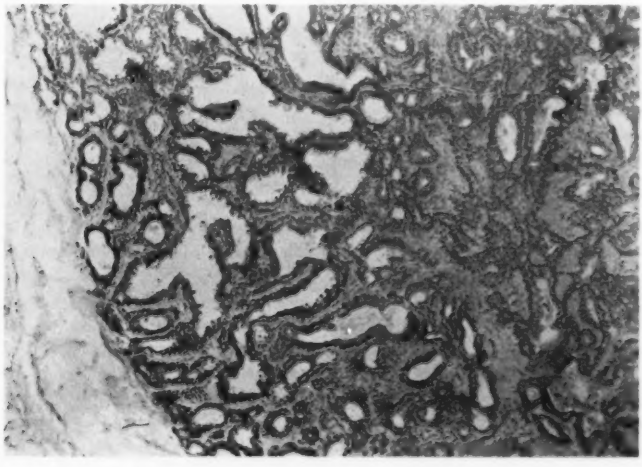

Fig. 1.—Nevus syringadenomatosus papilliferus. Low magnification (150 ×). Cystic spaces enclosing villus-like projections.

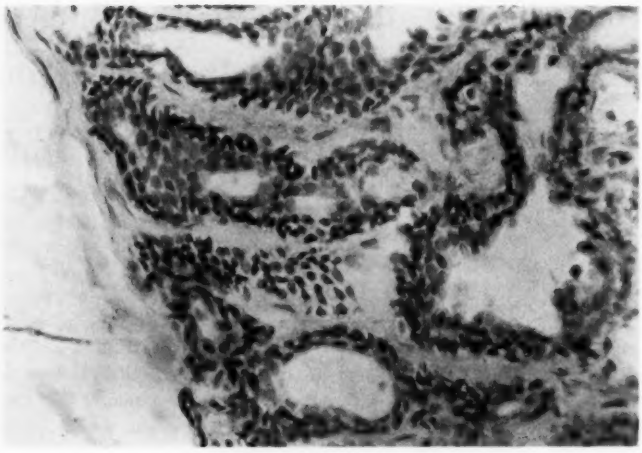

Fig. 2.—Nevus syringadenomatosus papilliferus. High magnification (615 ×). Dilated cystic structures lined by two layers of cuboidal-shaped cells.

Summary

A patient with a single lesion of syringadenomatosus papilliferus of the hairy scalp resembling a sebaceous cyst is reported.

140 E. 54th St.

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Special Small Knives for Minor Dermatologic Surgery

Their Value in the Performance of Small Biopsies and in Removal of Small Milia

LEON GOLDMAN, M.D., and ROBERT H. PRESTON, M.D., Cincinnati

Because of its simplicity and expediency, the small punch biopsy has been popular in dermatology for some time. However, there have been some objections to the use of this, especially on the face. Patients are concerned especially with the deep-depressed scars which result from the use of the 4 mm. and even the 2 mm. punch. Even with continued sharpening, the 2 mm. punch still produces some compression of the edges of the excised small bit of tissue so that it may be difficult to interpret this compression zone on some sections.

Submitted for publication May 14, 1958.

Special knives designed by Noel Robbins, Robbins Instruments Company, Chatham, N. J.

From the Department of Dermatology of the University of Cincinnati College of Medicine.

For years we have been using, especially on facial lesions, a technique which provided small, thin, but deep biopsies with a minimum amount of scarring. Originally we used small pieces of razor blade secured in a small-mosquito hemostat. This was unwieldy to use. Four years ago we devised a surgical knife by fixing a small piece of a razor blade in the handle used for the insertion of wood-carving knives. Recently a new handle has been devised which is more efficient and is easier to use.

The ideal biopsy specimen, especially from about the face, should be small, narrow, and deep. This special knife, with its thin blade, much thinner than even the smallest available scapel blade, does give us such a biopsy. These microblades are disposable. The handle may be sterilized in cold

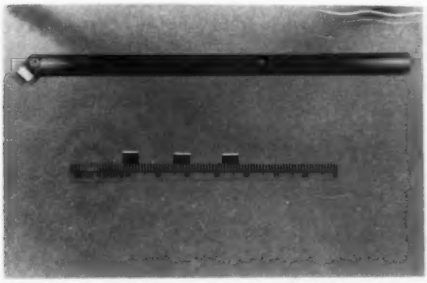
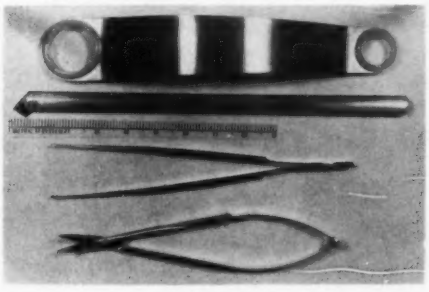


Fig. 1.—Special small knife for performance of small-type biopsies with the special replaceable blades.

germicidal solutions. The replaceable blade can be sterilized with alcohol. The exact site of the biopsy, after cleansing of the skin, is marked off with a 2% aqueous brilliant-green solution. Local anesthesia is then used to infiltrate the skin. The fine point of the knife cuts well into the skin and cuts deep enough into the skin. An assistant holds cotton applicators firmly to the side of the wound for better hemostasis. In some circumstances the pressure ring instrument can be used also to secure hemostasis. After the cut is made deeply enough, a fine-tooth eye forceps is used to pick up one end of the skin and then a fine curved-eye scissors is used to cut out the section at the required depth. The curvature of the scissors allows the specimen to rest on the blades. The tissue is put immediately on filter paper with the cut end down. If it is put on filter paper immediately and not on gauze, it sticks to the paper much better and does not come off in the formalin solution; also, the gauze threads do not interfere with the sectioning. The wound is then pressed together; may be sprinkled with a little absorbable gelantin sponge (Gelfoam) powder; adhesive strips are put across. On the face, transparent adhesive may be used. No sutures are necessary.

Fig. 2.—Detail and set-up for small biopsies with the special knife, small forceps, small curved scissors, and pressure ring for hemostasis.



The technician in the pathology laboratory must be familiar with the handling of small bits of tissue; otherwise the prepared tissue will be lost or not be oriented correctly. The tissue should be handled by the technician under a large magnifier, possibly a magnifier on a stand. A single drop of India ink at the edge of the filter paper may help in the orientation of this tissue. In our experience, these small deep biopsies have been found especially valuable about the tip of the nose, about the cheek area and eyelids, neck and dorsum of the hand.

Another type of knife utilizing the same general type of handle has been developed for the removal of tiny milia. For many of our women patients even the tiniest milia represents a serious challenge to their beauty so one is forced to remove these milia. In the soft tissues about the eyes this may be difficult at times. The special blade on this tiny milia knife can both incise the skin over the milia and spear the milia. To secure adequate removal, the skin is held tense with the fingers of one hand. A long cut is made in linear fashion above the milia and along the lines of cleavage or of wrinkling. This incision must be long enough. The milia is dissected out if necessary and then removed. With the use of binocular eye loups or the skin microscope even the smallest disturbing milia can be removed successfully.

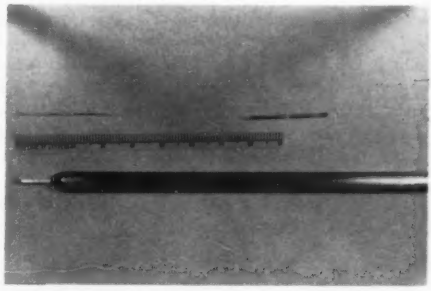


Fig. 3.—Special knife for removal of tiny milia.

Department of Dermatology, Cincinnati General Hospital.

The Oil Bath

JOHN M. KNOX, M.D., Houston, Texas; MARK ALLEN EVERETT, M.D., Oklahoma City, and ARTHUR C. CURTIS, M.D., Ann Arbor, Mich.

The beneficial effects derived from applying oil to the skin have been known for centuries. The Bible frequently speaks of "anointing the skin with oil." In an attempt to find a simple, effective, and esthetically pleasing method of lubricating the entire body surface, we formulated and introduced a practical oil bath. This investigation revealed that by adding a properly selected surface-active agent to an oil, the oil will disperse to infinity when stirred in water. This oil bath can be easily compounded by any pharmacist or physician.[1] Thus, a truly practical oil bath was developed.

Although other surface-active agents can be utilized, the oil-soluble alkyl aryl polyether alcohols * are completely satisfactory. They are nonionic and relatively nonsensitizing surfactants. When our exhibit was presented, no statements were made regarding therapeutic results obtained with the oil bath. For the last four years the oil bath has been prescribed for various dermatological diseases and a few indications and contraindications have been established. After studying hundreds of patients who have used the oil bath, the following observations have been made.

Submitted for publication June 9, 1958.

Departments of Dermatology, Baylor University College of Medicine, Houston, Texas (Dr. Knox), University of Oklahoma School of Medicine, Oklahoma City (Dr. Everett), University of Michigan Medical School, Ann Arbor, Mich. (Dr. Curtis).

* These chemicals may be obtained from Rohm and Haas, Philadelphia (trademark Triton) and from Antara Chemicals Division, General Aniline and Film Corp., New York (trademark Igepal).

The most spectacular and gratifying results have been in the treatment of xerosis, pruritus hiemalis, and mild to moderately severe ichthyosis. However, just as oily or greasy medications irritate or aggravate an acute dermatitis, the oil bath will often irritate inflamed skin. When a subacute dermatosis becomes a dry, chronic dermatosis, the oil bath is usually beneficial. The same care and caution should be used in switching from a drying colloidal bath to the oil bath as is used in changing from a drying, topical application to a lubricating preparation.

Although various vegetable oils and U. S. P. liquid petrolatum, have been used extensively, it has not been determined which, if any, is the oil of choice. To date, we have known of no incidence of epidermal sensitization to an oil or to the surfactant. Occasionally a patient has developed oil folliculitis; however, the condition promptly cleared on discontinuance of the medication. From the esthetic standpoint, patients have readily accepted the oil bath and complaints have been very infrequent.

Conclusion

The oil bath is an excellent therapeutic agent which is easily prepared and is effective in the treatment of selected dermatological conditions in which the skin is abnormally dry but not excessively inflamed.

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Treatment of Psoriasis with Riboflavin

BENCEL L. SCHIFF, M.D., Pawtucket, R. I., and ARTHUR B. KERN, M.D., Providence, R. I.

The therapeutic effects of riboflavin in psoriasis have recently been studied by several investigators. Their results are rather varied. Luscombe[1] reported marked improvement in 45% and improvement in 43% of the cases he followed and concluded that this form of therapy was a welcome addition to our armamentarium. Sulzberger and Baer,[2] who prescribed riboflavin by mouth to a great number of psoriatic patients, did not observe any significant improvement. Welsh and Ede[3] administered riboflavin orally and parenterally to a group of 348 patients with psoriasis but failed to produce any noticeable response. We studied a series of psoriatics to whom riboflavin was given orally and parenterally. The results are herewith submitted.

Ninety patients with chronic psoriasis were treated. Seventy-seven were given weekly injections of 1 cc. of aqueous solution containing 50 mg. of riboflavin-5-phosphate sodium (equivalent to riboflavin 35 mg.)* over a period ranging from one to four months. Forty of the seventy-seven patients also received riboflavin orally in dosage of 7.5 mg. three times daily. Thirteen patients received 1 cc. of the riboflavin solution intramuscularly daily for a period of four months. Of the 90 patients, 33 showed some improvement; 57, no improvement. A relief of itching was noted in some of the 57 patients who showed no objective improvement. Patients receiving daily injections showed no greater benefit than did those receiving weekly injections. The addition of orally administered riboflavin failed to have any demonstrable effect.

Submitted for publication May 13, 1958.

From the Department of Dermatology, Boston University School of Medicine (Herbert Mescon, M.D., Professor); Assistant Clinical Professor of Dermatology (Dr. Schiff) and Assistant Clinical Professor of Dermatology (Dr. Kern).

* Hyrye for this study was supplied by S. F. Durst & Co., Inc., Philadelphia, Pennsylvania.

Summary

Thirty-eight per cent of a series of 90 psoriatics treated with riboflavin showed some improvement; sixty-two per cent showed none. On the basis of these results it is concluded that riboflavin is of little value in the management of psoriasis.

351 Armistice Blvd., Pawtucket (Dr. Schiff)

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Triamcinolone Acetonide — A Highly Effective New Topical Steroid

J. GRAHAM SMITH Jr., M.D.; RAYMOND J. ZAWISZA, M.D., and HARVEY BLANK, M.D., Miami, Fla.

Triamcinolone acetonide, recently synthesized by Fried et al.,[1] has an anti-inflammatory effect 40 times as great in animals as cortisone or hydrocortisone. It is the purpose of this report to give the results of a preliminary evaluation of this highly active steroid as a topically applied therapeutic agent.

Submitted for publication June 10, 1958.

From the Division of Dermatology, Department of Medicine, University of Miami School of Medicine. Dr. Smith is a Special Post-Doctoral Research Fellow of the National Institute of Arthritis and Metabolic Diseases.

Materials and Methods

Triamcinolone acetonide* was supplied initially as a 0.05% and 0.1% lotion. These two creams were compared in a double-blind study with 0.1% fludrocortisone (fluorohydrocortisone) cream. The

* Supplied by E. R. Squibb & Sons as Kenalog.

Comparison of One-Tenth Per Cent Triamcinolone Acetonide with One Per Cent Hydrocortisone Topically

Diagnosis	Triamcinolone Acetonide Better Than Hydrocortisone		Triamcinolone Acetonide Equal to Hydrocortisone		Hydrocortisone Better Than Triamcinolone Acetonide		Neither Effective		
	Subjective	Objective	Subjective	Objective	Subjective	Objective	Subjective	Objective	Total
Atopic dermatitis	18	19	4	3					22
Chronic eczematous dermatitis	23	23	9	10	2	1	1	1	35
Chronic dermatitis hands & feet	10	10	5	5	2	2			17
Dermatitis venenata	5	4	3	4					8
Stasis dermatitis	3	3	1	1					4
Intertrigo	2	2							2
Dyshidrosis			1	1			2	2	3
Lichen simplex chronicus	7	7							7
Insect bites	1	1	1	1					2
Nummular eczema			1	1					1
Miliaria rubra	1	1							1
Seborrheic dermatitis	4	4	2	2					6
Dermatophytid reaction	1	1							1
Total	75	75	27	28	4	3	3	3	109

preliminary evaluation revealed the triamcinolone acetonide to possess such a high degree of effectiveness that a second double-blind symmetrical paired comparison study[2,3] was performed. Hydrocortisone in 1% concentration was supplied in lotion, cream, and ointment forms and compared with 0.1% triamcinolone acetonide in the same bases. Neither the investigator nor the patient knew the identity of the preparations, one of which was applied to lesions on one side of the body and the other, to contralateral similarly involved sites. At any one time only a single type of base was used for each medication. Patients were treated for periods of one week to one month or longer.

Results

The Table shows the comparison of 0.1% triamcinolone acetonide with 1% hydrocortisone topically in a series of 109 patients. These preparations were evaluated in a double-blind study as to their effectiveness, and the identity of the preparations was not known until the completion of the study. Each patient was asked to evaluate the preparations, and the examining physician also evaluated the sites of application for objective evidence of differences of effectiveness. In 68.7% (75 of 109), 0.1% triamcinolone acetonide was more effective both subjectively and objectively than 1% hydrocortisone, and in only 3.7% (4 of 109) and 2.8% (3 of 109) of the cases was there subjective or objective evidence respectively of the superiority of 1% hydrocortisone. Figures 1 and 2 show strikingly the differences observed in the objective superiority of triamcinolone acetonide over hydrocortisone in two patients.

Patients treated unsuccessfully with many other topical steroids showed for the first time complete regression of their lesions after treatment with triamcinolone acetonide, and the response was usually dramatically accelerated.

Weights of several patients were followed, with no evidence of gain or loss. Following extensive local use of 30 ml. of 0.1% triamcinolone acetonide

Fig. 1.—Wrists of 25-year-old patient with long history of atopic dermatitis. Left wrist treated for one week with 0.1% triamcinolone acetonide cream; right wrist treated simultaneously for one week with 1% hydrocortisone cream.

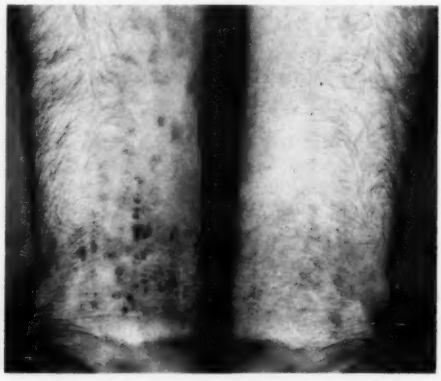

Fig. 2.—Abdomen of 8-year-old patient with atopic dermatitis. Left side of abdomen treated for one week with 0.1% triamcinolone acetonide cream; right side treated simultaneously for one week with 1% hydrocortisone cream.

daily for six days, in one patient, there were no changes in chloride, sodium, and potassium serum electrolytes or in body weight. No cases of sensitivity were observed. Two patients complained that the triamcinolone acetonide in a lotion base burned, and one stated that the hydrocortisone lotion burned.

Summary

In a double-blind symmetrical paired comparison study, 0.1% triamcinolone acetonide was compared with 1% hydrocortisone topically in lotion, cream, and ointment bases in a series of 109 patients. In this concentration triamcinolone acetonide was found to be a highly effective steroid and, in general, was superior to 1% hydrocortisone. No effects suggestive of systemic absorption or toxicity were observed.

Drs. J. J. Goodman; J. H. Hicks, and W. M. Sams supplied data concerning some of the patients included in this study.

University of Miami.

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Ultraviolet Light Therapy

Utilization of Tubular Fluorescent Lamps in a Cabinet for Generalized Simultaneous Irradiation

MURRAY C. ZIMMERMAN, Whittier, Calif.

Previously available ultraviolet light emitters have been "point," or small-area, sources. These require four to six exposures, averaging three to five minutes each, to irradiate the entire body evenly. Hence, a single generalized ultraviolet irradiation treatment keeps a room and a supervising nurse (or doctor) occupied for 20 to 30 minutes.

This article is written for the following purposes:

(1) To describe an ultraviolet cabinet, especially designed to give generalized, head-to-toe ultraviolet irradiation in a single exposure, with a minimum of supervision, and in minimum elapsed time (i. e., 2 minutes vs. 20 minutes)

(2) To discuss the technique of use of this cabinet

(3) To discuss the results and complications after four years' experience using the cabinet

(4) To provide detailed instructions for the reproduction of the cabinet

(5) To record the characteristics of a new ultraviolet light source (a 48-in.-long, tubular fluorescent lamp used in this cabinet)

(6) To compare this with previously available ultraviolet light sources

(7) To discuss briefly other possible installations of this tubular, fluorescent ultraviolet light source for dermatologic use

The Ultraviolet Cabinet

The ultraviolet cabinet hereunder described was built to order in a remodeling of my offices four years ago.*

This cabinet is 3½×2¾ ft., set in a 5½×6 ft. dressing room (Fig. 1). It has two 4 ft. fluorescent tubes set vertically at each corner. The tubes are turned on by a 15-minute automatic electric timer switch, similar to the familiar x-ray timer. The patient is observed through an ultraviolet-opaque observation window.

The surrounding dressing room is convenient but not necessary. The cabinet arrangement can be used in any closet bigger than 2½×2½ ft. or in a 2½ ft. corner of any treatment room. (Several local dermatologists have already copied this and are pleased with their results.)

Submitted for publication May 13, 1958.

From the University of Southern California School of Medicine, Department of Medicine (Dermatology [Maximilian E. Obermayer, M.D., Chairman and Head of Department]).

* Dr. Theodore Cohen, of San Bernardino, gave me the original idea for this cabinet.

Technique of Use

The patient is escorted into the dressing room, told to disrobe completely except for shoes and socks, then to knock on the outside door for the nurse. As the nurse comes into the dressing room, the patient steps into the ultraviolet cabinet and shuts the door.

Skolex Sunscreen Cream is smeared thinly on the nipples of all patients and on the glans of circumcised males. Since the tops of the lights are 5 ft. 4 in. from the ground, patients less than 6 ft. tall without facial lesions may wrap a towel around the head and lock hands behind the neck to hold it. If a towel is not used, the patient wears protective dark goggles. The nurse turns on the timer and as the fluorescent tubes flash on checks through the observation window that the tubes are burning properly, that the patient has goggles on, and that he is properly positioned. (The dressing room has no windows and is also used as a dark room for Wood's light examination.)

After the automatic timer is set, a second, separate, spring timer is set to ring a bell at the same time as the built-in timer shuts off the lights. The patient is told to leave the cabinet and dress himself when *either* the bell rings *or* the ultraviolet lights go out. This "double check" guards against a possible failure of one timer unit (which has never happened) and prevents an inadvertent overexposure. It allows the nurse to leave.

The patient stands in the center of the cabinet, facing the rear wall, feet slightly apart. He either stands still or alternately raises his knees to expose the medial thigh areas, if these are involved. The hands are locked on the occiput. This gives extra exposure to the elbows and permits exposure of the lateral thorax and axillae.

Exposure Times

Thin-skinned blondes or redheads are started at one minute exposure; dark brunettes, at three minutes; Mexicans or Sicilians, at five minutes.

Since tolerance develops, as to any ultraviolet exposure, exposure times are increased if the patient has not had a sufficient reaction from a given dose. Exposures are given once or twice weekly. Exposure rarely exceeds 12 minutes, except on Mexican patients, even after maximum ultraviolet tolerance has developed, to produce as much reaction as patients can comfortably endure. With this light source, it takes very little increase in time to increase the resultant reaction from faint erythema to severe erythema (Fig. 4).

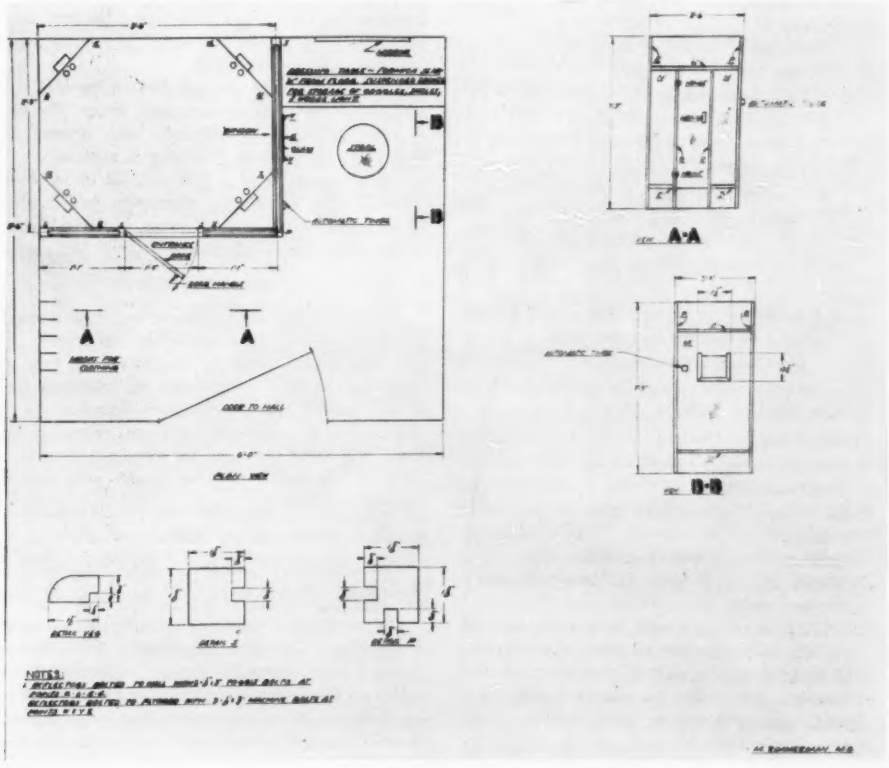
Results

We have used the ultraviolet cabinet for several thousand treatments. Patient acceptance has been excellent. Pityriasis rosea, psoriasis, atopic eczema, "neurodermatitis," and other generalized or diffuse dermatoses have responded at least as well as to either "cold" or "hot" quartz therapy. Some of our tense, nervous patients specifically ask for the "barbecue pit" because they say exposure relieves their tension, just as sun bathing does.

Pityriasis rosea cases gave an unsought "control." When the cabinet was first used, all patients stood still. The first pityriasis rosea cases cleared rapidly and completely (usually in three to five treatments at three-day intervals), except on the medial thighs, where the skin was not exposed. Lesions on these areas remained completely unchanged. Having the patient raise his knees alternately and slowly to the chest—a technique inaugurated after observing this—exposes the medial surface of the thighs to the ultraviolet rays and also, by keeping the patient moving, prevents any possible fainting attack from postural hypotension.

After three years' use, we replaced the starters for all eight tubes. These cost 25 cents each, and their replacement took three minutes, like putting in a new light bulb. Nothing has been broken, either by accident or by a patient. The tubes now require about one-third longer exposure time for the same degree of erythema than they did at first use. Since this is a question of setting the timer for an extra minute or two, we have not yet replaced these tubes with new tubes.

Fig. 1.—Detailed drawing of ultraviolet cabinet. Lettering code described in text.



Complications

The only untoward incident in four years' operation occurred in treating a patient with chronic, generalized psoriasis. He was a veteran of many dermatologists and of many exposures in the cabinet. One day he took off his glasses as soon as the nurse left and read by the light of the eight lamps for a 12-minute exposure. From this folly, he developed a mild, actinic keratoconjunctivitis eight hours later, which was relieved completely by one application of hydrocortisone ophthalmic solution.

Details of the Cabinet

To order (see Fig. 1 for placement)

(1) Lumber yard

⅜ in. plywood

M—1 piece 31½×65 in., with 8×11 in. vertical hole cut, 12 in. from side edge, 14 in. from top

N—2 pieces 12×65 in.

2×2 in. stock (true dimensions 1⅝×1⅝ in.)

P—1 piece, *floor to ceiling height,* rabbeted on adjacent sides, with ⅜×⅜ in. slot. (Shown as 7 ft. 9 in. on diagram)

S—37 ft., rabbeted on one side only, ⅜×⅜ in. center slot

Pieces of *S* better cut to fit in office during assembly (see Fig. 3)

L 1 piece, 40 in. long

Q 2 pieces, each 76 in. long

R 2 pieces, each 64 in. long

E 1 piece, 11¾ in. long

T 1 piece, 10¼ in. long

U 2 pieces, each 32 in. long

VG 40 in., 1⅝×¾ in. molding, with ¼×¼ in. notch on corner (*VG* on Fig. 1 shows cross section)

V 2 pieces of the above molding 13¼ in. long, mitered 45 degrees at lower ends

G 1 piece of the above molding, 11¼ in. long, mitered 45 degrees at both ends to 8¼ in.

1 Slab door, 14¾×66 in.

(2) Glass store

1 piece dark-blue glass, 8½×12×⅛ in.

(3) Hardware store

Small tube of all-purpose glue, or cement, to glue

Aluminum foil—1 roll (household type)

12 3×⅜ in. toggle bolts (to bolt reflectors to plaster walls)

12 ¾×⅜ in. machine bolts, with nuts and washers (to bolt reflectors to plywood walls)

4 clothing hooks for wall of dressing room

2 hinges and 1 handle for cabinet door

Wood screws and nails to fasten cabinet together

1 pt. white lead paint (flat)

(4) Electrical supply store

16 2 SF wire, 25 ft., plus distance from cabinet to electric outlet

1 heavy-duty electric plug, two-prong, male

1 15-minute electric switch timer; make "on"; break "off"

4 2-unit 40 watt, fluorescent fixture, with medium bi-pin bases, and eight 40-watt starters for fixtures

8 48 in. fluorescent, Westinghouse 40 watt "Sun Lamps," FS40T12

(5) Machine shop

4 aluminum reflectors, 14½×48 in., each drilled to admit starters and bases of fluorescent fixtures and to allow fastening of fixtures to their posterior sides

(6) Drug store

1 pair protective dark goggles

The wood used to make the cabinet costs about $10 at any lumber yard. If the plywood is ordered pre-cut, as specified, and the rabbeted 2×2 stock is delivered in long lengths, needing only pieces cut off for assembly, the installation of the cabinet will require a drill, hammer, nails, crosscut saw, screwdriver, and pliers. It is simple and suitable for do-it-yourself addicts. It should take a carpenter about four hours. Filling in cracks, sanding, and painting the entire unit will take a painter about four hours. It should be painted before the lights and reflectors are installed.

The electric units are installed in parallel with each other and with the automatic timer. The wire is run behind the reflectors and around the bottom of the cabinet. The plug is attached to the end and inserted into a 110 volt, 60 cycle, A. C. outlet. After installation, aluminum foil is glued to all inside wall and door areas in the cabinet to increase ultraviolet reflectance.

Reflectors †

Alzak is an aluminum reflector material, specially polished for maximum ultraviolet reflectance. Its use cuts down markedly the exposure time by reflecting outward components of radiation back at the patient. Since reflectance decreases as the wavelength is shortened, optimum reflecting material for ultraviolet cuts the exposure time to as little as one-third of what would otherwise be necessary (Table).[1]

Light Source

The ultraviolet source is eight Westinghouse fluorescent "Sun Lamps," 48 in. long, 40 watt,

† My reflectors were designed by Mr. Bernard F. Cohlan, Consulting Engineer, 2850 Moraga Drive, Los Angeles 24. Losses in intensity from increased distance and decreased angle of incidence are balanced by reinforcement from adjacent light sources.

Relative Reflectance of Ultraviolet by Various Surfaces, Demonstrating the Increased Efficiency of Alzak Reflectors

	Approximate per Cent Reflectance	
	For Light	For 2967 A.
Alzak		
Diffuse	78	65
Specular	85	71
Chrome steel	56	41-44
Chromium-plated metal	65	62
Nickel-plated metal	61	32
Stainless steel	60	33
White lead paint, flat	80	27
White porcelain enamel	70	7

FS40T12. Two of these lamps fit into each of four standard bi-pin, double socket, 48 in. fluorescent fixtures. These 40 watt fixtures, including ballasts (transformers), wiring, and underwriter-approved shielding, are items obtainable at any electrical supply store.

Each of the eight lamps is a standard "hot cathode" fluorescent tube, containing at high vacuum (3.2 mm. of mercury) a small quantity of argon gas and mercury. A high-voltage, low-amperage, electrical current passing through the tube generates a glow discharge at 2537 A. *inside* the tube. This strikes the special phosphors coating the inside walls of the tube, exciting the phosphors to *fluoresce* (i. e., to radiate a continuous spectrum of longer wavelengths [2800-3500 A.] *outside* the tube). Heat production is minimal; the tubes can be touched at any time without discomfort. The lamps are warranted for five thousand 15-minute treatments, without replacement.[2]

This tube differs from the standard, illuminating fluorescent lights in two respects:

1. The phosphors are selected to radiate an ultraviolet spectrum, continuous from 2800 to 3500 A., instead of radiating visible light. The small amount of visible light produced (longer than 3900 A.) is soft blue in color.

2. The tube is made of a special glass (synthetic quartz) allowing the passage of ultraviolet wavelengths longer than 2750 A. (Regular glass stops the transmission of wave lengths shorter than 3200 A.)

Figure 2 shows the continuous-spectrum emission of this light source, 90% between 2800 and 3100 A. Figure 3 compares it with other ultraviolet spectra. The definition of "sun lamp" by the Council on Medical Physics of the American Medical Association,[6-8] for safe home use without the supervision of the physician is, "The spectral range of wavelengths from sunlamps shall be limited largely from 2900 to and including 3132, and shall not include an appreciable amount of ultraviolet of wavelengths shorter than 2800 Ångstrom."

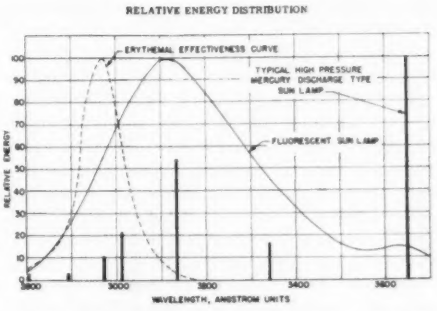


Fig. 2.—Comparative spectra of artificial ultraviolet sources.

Previous Ultraviolet Light Sources—a Comparison

Very hot bodies and ionized gases emit ultraviolet rays. Previous artificial sources of ultraviolet light may be grouped into three main classes:

(1) carbon arc

(2) mercury vapor arc ("hot" quartz)

(*a*) bulb-type sun lamps

(3) mercury vapor glow discharge ("cold" quartz)

(*a*) modified mercury glow discharge

Carbon Arc.—This was the first source of artificial ultraviolet, now superseded in office practice. Basically, it consists of two rods (electrodes) of carbon mixed with traces of metals. One end of each rod is connected to a source of electricity. The opposite ends of the rods are in contact with each other. When the rods are slightly separated, electricity flows across the gap in an arc, producing intense heat (over 3000 C). The incandescent glow from the ends of the electrodes emits a continuous-spectrum radiation, with all wavelengths present. The arc itself produces spectral lines, or bands, due to ionization of the electrodes (Figs. 2 and 3). Selection of different types of carbon, with admixtures of trace metals, makes it possible to have a high percentage of long or short wave ultraviolet, or of visible light, spectral bands, as desired. Modern carbon arc lamps do not have the problems of fumes and flying sparks, but are messy, require carbon replacements, and produce considerable heat. Because of the elaborate ventilating and screening required, these lamps are relatively expensive.

Mercury Lamps.—Mercury, when vaporized by electron activity (either heat or electrical flow), emits a spectrum rich in intense linear bands in the ultraviolet. The mercury is encased in a quartz tube for two reasons:

1. Quartz (silicon dioxide) allows the transmission of all ultraviolet wavelengths longer than

1800 A. (Glass transmits only wavelengths longer than 3200A.)

2. Quartz is extremely heat-resistant. (Quartz is also expensive, brittle, hard to work, and fragile.)

"Hot" Quartz vs. "Cold" Quartz.—Vapor pressure of mercury in a quartz tube is determined by the temperature. Vapor pressure and temperature determine spectral emission. For this reason, mercury vapor arc lamps, which operate at high vapor pressure (1 to 10 atmospheres) and high temperature, are referred to as "hot" quartz lamps. Mercury glow discharge lamps, which operate at low pressure (0.001 atmosphere) and low temperature, are referred to as "cold" quartz lamps.

Mercury Arc ("Hot" Quartz) Lamps.—These have been the most widely used source of artificial ultraviolet light because of ease of handling and low current usage. They have disadvantages of expense and of requiring three to five minutes to warm up to full output and then three to five minutes of cooling off before they can be restarted. They must be equipped with either a circulating water or air cooling system to dissipate the heat they generate.

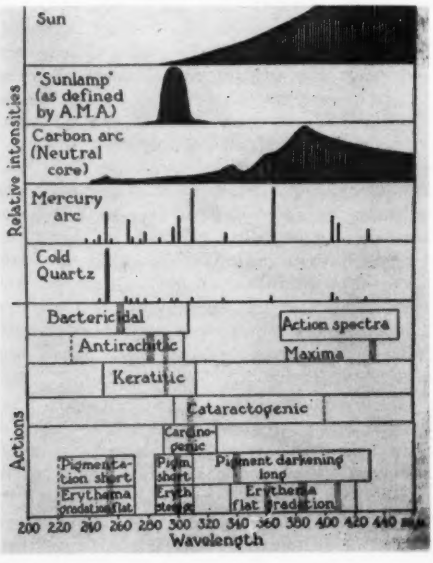
These lamps consist of a quartz tube exhausted of air, containing neon and a drop of mercury. When the current is turned on, the mercury forms an electric contact. The heat generated vaporizes the mercury. This assists the production of ultraviolet, visible light, and a small amount of infrared. In this high-pressure mercury spectrum, 80% of the ultraviolet energy is in 12 wavelengths and 20% in others. Nine per cent of the energy is at 2537 A. The other principal wavelengths are at 2482, 2652, 2700, 2752, 2803, 2894, 2967, 3025, 3130, 3341, and 3660 A. (Figs. 2 and 3).

R S Type Sun Lamps.—These consist of a small quartz tube inside a large Corex D glass, or Corning glass bulb. (This special glass allows the exit of ultraviolet wave lengths longer than 2800 A.) The outer bulb is lined on the inside base with aluminum, for increased reflectance. A standard tungsten filament, as in any incandescent lamp, becomes incandescent when the current is turned on. After a minute or two, the heat of this filament vaporizes the mercury in the inner quartz bulb. This activates a switch inside the bulb, which starts a mercury arc in the inner quartz tube. The resistance of the tungsten filament automatically limits the current to the mercury tube electrodes, saving the expense of a transformer. This 275 watt bulb puts out mercury excitation bands 2894 A. and longer in the ultraviolet, as well as visible light and infrared from the tungsten filament. It is an inefficient but cheap ultraviolet source.

Mercury Glow Discharge ("Cold" Quartz) Lamps.—These lamps consist of a narrow quartz tube bent in a circular or hexagonal grid for irradiation of large areas or shaped in tubes and rods to use in body orifices. The quartz tube is evacuated of air to a high vacuum (0.001 atmosphere) and contains neon gas and mercury vapor. A transformer steps up standard 110 volt current to about 2500 volts. The resulting flow of electrons across this high potential produces a glow discharge. Because of the high vacuum, little amperage is necessary to produce the current. Consumption of electricity is very low; hence the tube remains cold. Full light emission is present within one minute, 90% in the spectral line of 2537 A. (Figs. 2 and 3). No cooling-off period is necessary before reuse.

Modified Mercury Glow Discharge Lamp.—This is the Westinghouse Fluorescent Ultraviolet Tube described in this article.

Fig. 3.—Comparative graphing of wavelengths and effects of available ultraviolet sources.



Physiologic Effect of Ultraviolet Wavelengths

The wavelength 2537 A. approximates the absorption and action spectrum of nucleoprotein. Damage to cell nuclei produces erythema without subsequent tanning. Tripling or quadrupling the exposure to a cold quartz ultraviolet source increases only slightly the resulting erythema (Fig. 4).[8] In clinical terms, there is an extremely wide margin of safety (or time) between a minimum or mild erythema dose, and a severe erythema dose.

The wavelength 2967 A. approximates the absorption and action spectrum of cytoplasm. It produces erythema and triggers the first step in

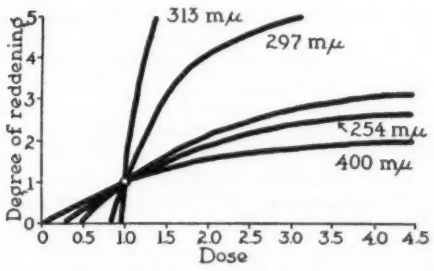


Fig. 4.—Graphing of erythema response to ultraviolet wavelengths.

tanning. It is the peak wavelength in the ultraviolet cabinet, as here described.

Figure 4 shows the rapid increases in erythema response from minimal increases in 2970 A. exposure. Slight increase in exposure time, producing exponentially increased erythema response, is a great time-saving factor in office use, as the patient develops ultraviolet tolerance.

The wavelengths 3341 and 3660 A. approximate the shortest absorption and action spectra of photosensitizing compounds in tars and in most photodynamic compounds. They allow photosensitization to be used therapeutically, as in the Goeckerman treatment of psoriasis (3900-5000 A. are the main absorption and action spectra of compounds in tars).

Advantages of Fluorescent Ultraviolet Light Source and of Cabinet

1. Time saving

(*a*) The entire body can be irradiated evenly at one time, without supervision, in about one-fifth the time necessary by other techniques, hence at lower cost in nursing time, and faster turnover in use of a room.

(*b*) No warm-up period is necessary for these lamps. Maximum ultraviolet output is achieved within 30 seconds.

(*c*) No cooling-off period is necessary before reuse of the lamps.

(*d*) Increased erythemal response achieved with very slight increase in exposure time.

2. Economy of installation

(*a*) The entire set-up, as outlined here, should be installed for less than $400, a considerable saving over many other ultraviolet sources.

(*b*) A full-sized treatment room is not necessary, saving both square footage of floor space and the cost of furnishing and maintaining a room with treatment table, chair, etc.

3. Economical operation

(*a*) Long tube life (5000 treatments of 15 minutes each) for total of $100 in tubes (retail price).

(*b*) Easy maintenance (new tubes installed in 10 seconds as easily as putting in a light bulb).

(*c*) Standard fluorescent fixtures—can be worked on by any electrician—parts available at any electrical supply store. No waiting for factory replacement or factory-trained specialists to work on the unit.

(*d*) High efficiency (higher erythemal effectiveness per watt than any other ultraviolet source).

(*e*) No carbons to replace, as with carbon arc. No expensive quartz tubes to replace, as with "hot" or "cold" quartz sources.

(*f*) No complicated air- or water-cooling apparatus to break down.

4. Accident-free

(*a*) Rugged construction—no fragile and expensive quartz tube to break or to be broken by patients.

(*b*) Since the tubes are lateral to the patient, there is no chance of either spontaneous or induced breakage leaking hot mercury by gravity on a patient below the light source, with resultant thermal burn.

5. Cool operation

Lamps can be touched at any time. There is no heat dissipation problem in a small room and no danger of an accidental contact burn.

6. Therapeutic efficiency high (At least as effective as either "hot" or "cold" quartz therapeutically)

7. Broad uniform coverage

The 48 in. linear light source is ideal for the purpose of general irradiation. No "point" light source is suited to this.

8. No noise, no ozone smell

9. Physiologic wavelengths only

Same wavelengths as present in sunlight and in continuous spectrum.

10. May be used synergistically with photosensitizers (e. g., tar—shortest action spectrum about 3400 A.)

"Cold" quartz cannot be so used.

The automatic timer, and complete fixtures with fitted reflectors, ready to install, including eight lamps, may be purchased.‡ Alternately, similar units and lamps may be ordered from a local electrical supply house and reflectors may be made to order by a local machine shop.

Other Installations of Fluorescent Ultraviolet Light Source

For dermatologists who want a generalized irradiation source but who cannot or do not wish to remodel a room to get it, a 6 ft. high stand with a 24×32 in. base is available‡ (Fig. 5). The patient stands on the dark circle shown on the base center and revolves to face each of the five lighter circles at the periphery of the base as the auto-

‡ Don Cameron Company (Medical Supply Division), 1054 Broxton Ave., Los Angeles 24.

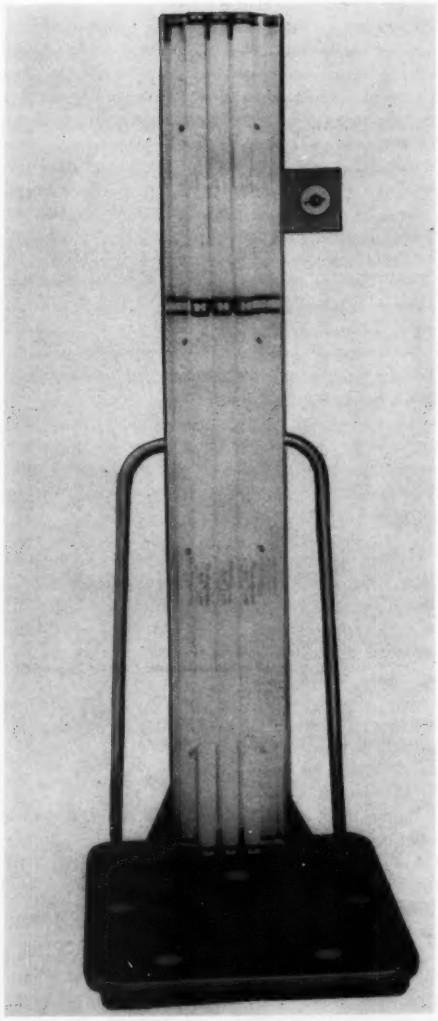


Fig. 5.—Tubular fluorescent ultraviolet unit.

matic timer clicks off the minutes. This unit can be set up in any treatment room. It takes up no more room than the 24×32 in. base, like a platform scale. It is equipped with three 48 in. lamps and three 24 in. lamps in front of an Alzak reflector. It will give generalized second-degree erythema in 10 minutes on a first exposure, allowing 2 minutes in each of the five positions, at 1 ft. distance. The wavelengths are, of course, the same as in the cabinet. Its only disadvantages are the increased time, the increased supervision, and the occasional reluctance of a modest patient to stand nude in an open room. Its use without supervision presupposes a patient intelligent enough to read numbers on the timer or on a clock and to turn to the next circle after a given elapsed time. It is better to have supervision with this unit, at least through the first treatments. With this unit, because of its 6 ft. height, all patients (except those on basketball scholarships) will require facial covering for at least part of their exposure, unless facial erythema is desirable. If only facial erythema is desirable, the upper lights can be turned on alone.

Summary

A 4 ft. tubular fluorescent lamp, with a continuous ultraviolet spectrum 90% between 2800 and 3100 A., is a cheap, uncomplicated, fast, and useful source of therapeutic ultraviolet for generalized irradiation. Its advantages and physical properties, incorporated in a specially designed cabinet for dermatologic use, are described. Instructions for making and using such a unit are given, along with a list of materials necessary.

Results and complications observed after four years of use are reported.

A comparison of wavelengths and effects of this and other sources of ultraviolet is given.

301 E. Hadley St.

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Correspondence

POLIOMYELITIS VACCINE AND RECURRENT HERPES SIMPLEX

To the Editor:—In the June, 1958, issue of A. M. A. Archives of Dermatology, p. 750, in my discussion at the Detroit Dermatological Society Meeting of Nov. 13, 1957, held in Ann Arbor, Mich., I discussed the use of poliomyelitis vaccine in such conditions as herpes simplex, herpes zoster, and aphthous ulcers, as well as in the case of periadenitis mucosa necrotia recurrens. At that time, I was unaware of any previous publication with regard to this therapy. However, in catching up on some of my back reading, I have come across a letter "to the Editor," published in *The Journal of the American Medical Association* (164:205 [May 11] 1957), entitled "Poliomyelitis Vaccine and Recurrent Herpes Simplex" and signed by Drs. Leon Adoni and Donald N. Tschan, of the Department of Dermatology, Temple University Medical Center, Philadelphia. In this letter, Drs. Adoni and Tschan mention their use of poliomyelitis vaccine in a case of recurrent herpes simplex, with two standard-dose injections of poliomyelitis vaccine, and also their observation that a technician, employed in the department of virology of Temple University Medical Center, attained relief with the accidental oral ingestion of poliomyelitis virus, following which he suffered no further recurrences of his herpes simplex.

Since Drs. Adoni and Tschan preceded me by some months, in making this observation, I wish you would publish this letter in the Archives to acknowledge this priority.

James R. Rogin, M.D.
1150 Griswold, Cor. State
Detroit 26.

CONTROL OF EMOTIONAL FACTORS IN DERMATOSES

To the Editor:—Critical correspondence may be instructive providing something new and authentic is added. Avoiding the possibility of belaboring trite statements, the observations contained in Dr. Morris Leider's letter in the A. M. A. Archives of Dermatology, July, 1958, issue, require in the nature of accuracy further comment. The repetitious statement that the skin is the largest organ in the body is metaphorical. It is the largest in the sense that it is continuous, encompassing, and visual. Other elements in the human structure may cover a larger area if placed end to end. In life most things are measured by size and comparison and are primarily based on a yard stick.

The word ***hubris*** is mentioned that the Greeks connotate "with a sort of pride." The etymological root is of Greek origin. The definition is "an insolent disregard of all moral laws and restraints." The word has crept into usage only lately and is not found in the older lexicons.

Charles Wolf, M.D.
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1 W. 81st St.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Morris Leider, M.D., President

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Nov. 21, 1957

Roentgen Radiation of Epitheliomas Situated Over the Cartilage of the Ear and Nose. Abstract of a paper delivered by Dr. Earle W. Brauer.

Dermatologists have for many years applied roentgen rays over cartilaginous areas in the treatment of both basal-cell and prickle-cell epitheliomas of the skin. Standard dermatologic texts as well as the current dermatologic literature present treatment schedules with little if any reference to the possibility of producing chondronecrosis as a complication of the radiotherapy. Despite this, many dermatologists are almost unconsciously reluctant to administer ionizing radiation in cancericidal dosage over the nose and ear. This reluctance may be created by the roentgenologic and biophysical literature rather than the dermatologic literature. In the former, painful chondronecrosis of the cartilages of the nose and ear following radiation therapy for skin cancer is clearly and frighteningly described.

It is theorized that complex biologic material has effective atomic numbers as follows: muscle 7.42, subcutaneous fat 5.92, and bone 13.8; air, by comparison, is assigned the number of 7.64. These materials absorb energy per electron as a function of approximately the cube root of the atomic number when exposed to radiation with a half-value layer between 0.3 mm. Al and 0.5 mm. Cu. Therefore, it is calculated that the energy absorption of a dose of 1 r to 1 gm. of air is 85 ergs; that of subcutaneous fat, only 46 ergs, but that of bone, 485 ergs. The differential in energy absorption in bone as compared to air is by a factor of 5.7!

The Physiotherapy Section of the New York Skin and Cancer Unit at the University Hospital of the New York University-Bellevue Medical Center has established a routine schedule for treatment of both basal-cell and prickle-cell epitheliomas of the head regardless of size or location as follows: The mass is shielded to not less than 5 mm. from its border of clinical activity; the quality of radiation is that represented by a half-value layer of 0.9 mm. Al; treatments of 680 r each are administered every other day; basal-cell epitheliomas receive five treatments, for a total of 3400 r; prickle-cell epitheliomas receive eight treatments, for a total of 5440 r.

An acute radiodermatitis usually begins before the treatment schedule is completed and tends to reach a peak about 18 to 21 days after the last treatment. Redness and edema are followed by necrosis of the skin. Since a through-and-through epidermatitis appears on the auricle and ala of the nose, it is more than likely that some *radiochondritis* takes place. In most instances the treated site heals within eight weeks in an uncomplicated fashion. In approximately 50 cases treated under my direction, no *chondronecrosis* has taken place. The number of cases followed for five or more years is insufficient to draw any conclusions regarding superiority or inferiority of this technique over other established methods for permanent eradication of skin cancers by radiotherapy, but the fact that cartilage is not permanently injured by radiation such as is described is proved.

I do not know why my experience, and similarly that of other dermatologists, is contrary to what should be expected from theoretical biophysics or the writings of general radiologists. One might speculate that the total energy absorption from radiation under 6000 r with half-value layer about 1 mm. Al is below some unknown critical point below which cartilaginous tissue can withstand the ionizing effect. It is not unusual for living tissue to follow *"all or nothing"* laws of activity.

Cases Illustrating Roentgen-Ray Therapy of Epitheliomas Overlying Cartilagenous Areas. Presented by Dr. Earle Brauer and Dr. Gerald R. Frolow (by invitation).

Case 1.—A 50-year-old man had a lesion 7 mm. in diameter on the helix of the left ear for approximately four years. The lesion was treated by desiccation and curettage at the time of biopsy, on Nov. 19, 1956. Histopathologic examination of the biopsy specimen revealed a prickle-cell epithelioma. The patient then received eight treatments of 680 r each of unfiltered radiation given three

Submitted for publication Jan. 20, 1958.

times a week, with factors of 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance, between Dec. 17, 1956, and Jan. 7, 1957, for a total of 5440 r. A radiodermatitis involving both sides of the helix appeared after treatment and took approximately three weeks to subside. It is now 11 months after treatment. There is neither recurrence nor untoward sequelae of the skin and cartilage.

CASE 2.—A 77-year-old man had a lesion 10 mm. in diameter on the right antihelix which was diagnosed as a prickle-cell epithelioma by histopathologic examination of the biopsy specimen. The patient received eight treatments of 680 r each of unfiltered radiation given three times a week, with factors of 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance, between April 9, 1957, and April 26, 1957, for a total of 5440 r. A through-and-through radiodermatitis of the ear cleared in approximately six weeks after treatment. It is now seven months after treatment, and there are no signs of recurrence or of undesirable sequelae of skin or cartilage.

CASE 3.—A 55-year-old man had a lesion 7 mm. in diameter within the pinna of the left ear which was diagnosed as basal-cell epithelioma by histopathologic examination of the biopsy specimen. The patient received five treatments of 680 r each of unfiltered radiation given three times a week, with factors of 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance, between Dec. 11, 1956, and Dec. 20, 1956, for a total of 3400 r. A mild radioreaction followed treatment. It is now 11 months after treatment, and all is well.

CASE 4.—A 74-year-old man had a lesion on the posterior aspect of the right ear, 2.5 cm. in its largest diameter, for approximately three years. Histopathologic examination of a biopsy specimen revealed a basal-cell epithelioma. Desiccation and curettage did not eradicate the lesion, and six months later the patient received five treatments of 680 r each of unfiltered radiation given three times a week, with factors of 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance, between April 23, 1957, and May 2, 1957, for a total of 3400 r. The resulting radiodermatitis subsided in approximately four weeks. It is now six months after treatment, and nothing is visible except a healthy scar.

CASE 5.—A 65-year-old man had a lesion on the tip of the nose, 5 mm. in diameter, for two months. Histopathologic examination of a biopsy specimen revealed prickle-cell epithelioma. The patient received eight treatments of 680 r each of unfiltered radiation given three times a week, with factors of 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance between March 22, 1956, and April 10, 1956, for a total of 5440 r. A mild radiodermatitis followed. It is now 19 months after treatment, and hardly anything but a normal nose is visible.

CASE 6.—A middle-aged man had a lesion 1.5 cm. in diameter on the right ala nasi for one year. Histopathologic examination of a biopsy specimen revealed basal-cell epithelioma. The patient received five treatments of 680 r each of unfiltered radiation three times a week at 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance, between Nov. 4, 1957, and Nov. 13, 1957, for a total of 3400 r. It is now one week after treatment. Mild inflammatory reaction is to be seen.

CASE 7.—A 72-year-old man had a lesion 7 mm. in diameter on the left side of the nose which was diagnosed as basal-cell epithelioma of uncertain duration. He received five treatments of 630 r each of unfiltered radiation three times a week, at 100 kv., 10 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance, between June 20, 1957, and June 28, 1957, for a total of 3400 r. It is now five months after treatment. There is little to see by way of abnormality.

CASE 8.—A 62-year-old woman had a basal-cell epithelioma removed from the right side of the nose in January, 1948, by desiccation. There was no recurrence in six and one-half years of follow-up. A new lesion of six months' duration on the *tip* of the nose was proven to be basal-cell epithelioma by histopathologic examination of a biopsy specimen. The patient received five treatments of 680 r each of unfiltered radiation, at 100 kv., 5 ma., half-value layer of 0.9 mm. of Al, and 20 cm. target-skin distance between Oct. 29, 1957, and Nov. 8, 1957, for a total of 3400 r. It is now two weeks after treatment. Mild inflammatory reaction is to be seen.

Discussion

DR. EDWARD H. MANDEL: My experience in the management of this type of epithelioma has not been as great as that of Dr. Brauer. However, I have seen some recurrences with this schedule in basal-cell epithelioma. I should like to suggest at this time that additional radiation be given in the form of two more skin units in the management of basal-cell epitheliomas and squamous-cell carcinomas. In view of this five-year study, if these doses are given in a few patients now we shall not have to wait an additional five years after completion of this study to evaluate another schedule.

DR. CHARLES WOLF: It is well to recall, especially in a report of this sort and brilliant as the results seem to be, that many basal- and prickle-cell epitheliomata can be treated by other

means, e. g., scalpel and electrosurgery. I do not deem x-radiation the treatment of choice, considering all the hazards and the complexity. This is not to say that x-radiation is not a valuable modality at times and in certain cases.

DR. ABRAHAM J. ORFUSS: I should like to emphasize that it is necessary to be aware not only of cartilage lying directly below a neoplasm, as in the wing of the ear, but also one must consider tissues far beyond. I am thinking of radiation of the nose and the relation of the septum to the path of radiation. In order to avoid radiation sequelae in underlying structures, it must be remembered to shield with lead inside the nostril or oral cavity in some instances.

DR. SAMUEL B. FRANK: I have seen one instance of perforation of the nasal septum after irradiation of an epithelioma on a wing of the nose. I regularly insert lead foil in the nostril, but with this practice I have still noted intense reaction on the mucous-membrane undersurface of the treated area. I wonder if the use of lead somehow intensifies x-ray effect on the mucous membrane in front of it.

DR. HARRY SHATIN: I should like to compliment Dr. Brauer on his presentation, and I wish to state that our findings at the Bronx Veterans' Administration Hospital tend to confirm his thesis that one does not have to fear injury to underlying cartilage when irradiating skin carcinomas, if proper precautions are taken.

We have been treating basal-cell and epidermoid carcinomas of the skin for 10 years with dosages based upon the Strandquist curve. Our general program for lesions under 2 cm. in diameter has been to administer 500 r daily, to a total dose of 5000 r. The physical factors are 100 kv., 1 mm. Al filter, half-value layer 2 mm. Al, target-skin distance 20 cm. We have treated lesions on the nose, ears, and eyelids, and at no time have we had any evidence of chondronecrosis, either early or late.

DR. EARLE BRAUER: There are innumerable irradiation techniques for the treatment of skin cancers; all have merit, and all can stand criticism. Our technique was "standardized" only to produce uniformity at a busy teaching clinic where many physicians prescribe for patients. A standard was necessary for teaching and to make evaluation possible at some future date. Our technique for treatment is not what is under discussion tonight; the point made is that this method does not produce chondronecrosis.

Naturally, there is an art in the application of all techniques, an art which is developed only with experience. Skill in proper shielding and beam angulation is as important to the success of this technique as skill in dissection and knot-tying is to the surgical operation.

Case for Diagnosis. Presented by DR. VICTOR H. WITTEN and DR. FRANK KRASNER (by invitation).

A 6-year-old boy was well until 9 months of age, when he developed a pneumonitis which failed to respond quickly to conventional therapy but which eventually subsided. A smear of the peripheral blood at that time showed a white blood cell count of 18,000, with 15% polymorphonuclear leukocytes. Since then the patient has had numerous hospital admissions, mainly for recurrent painful ulcerations of the tongue, buccal mucous membranes, and oral pharynx. No pathogens could be cultured from these lesions; systemic antibiotics were of no value in controlling the course of the lesions. When the patient was 3 years old, electrophoretic analysis of the plasma proteins showed the γ-globulin to be 2.6% (normal, 11% to 16%). The patient was given γ-globulin intramuscularly in courses of 10 gm. each, and the ulcerations disappeared.

Approximately one-half year later the ulcerations in the mouth reappeared and were resistant to γ-globulin therapy but responded somewhat to cortisone administered systemically. Because leukopenia (white blood cell count, 4000), neutropenia (polymorphonuclear leukocyte count, 4%), and splenomegaly were noted at this time, splenectomy was performed. Splenic tissue sections revealed normal tissue. The splenectomy had no effect on the course of the oral ulcers or on the polymorphonuclear leukocyte count. Thrombophlebitis and gangrene developed at the site of a surgical cutdown on a vessel for intravenous administrations and failed to respond to therapy. A midthigh amputation was required to save life.

When the patient was 4½ years old it was noted that his blood albumin was 2 gm. %, and although there was a normal total blood protein value it was made up mostly of α-globulin. The patient was admitted for study to the Rockefeller Institute for Medical Research. A skin eruption appeared for the first time which consisted of well-defined erythematous scaly plaques of various sizes. They varied in configuration from nummular plaques to lesions which were crescentic and annular. At that time the following diagnoses were considered: (*a*) atypical seborrheic dermatitis, (*b*) atypical atopic dermatitis, (*c*) lymphoblastoma. The skin lesions responded very well to Vioform ointment. Mycostatin in Plastibase was employed locally for the oral ulcerations, with good response.

One year ago the patient was found to have profound anemia (hemoglobin, 4.5 gm. %; albumin, 1.7 gm. %, γ-globulin, 5%). Examination of the gastrointestinal tract revealed a pedunculated polyp in the cecal region. A laparotomy performed in December, 1956, revealed, in addition to the polyp,

an infiltrating lesion, resembling a granulomatous process, involving the entire intestine wall, beginning at the terminal ileum and extending over most of the ascending colon. This entire portion of the intestinal tract was excised. Frozen section showed subacute arteritis with infiltration around the small arterioles. Fixed tissues revealed an identical picture. No specific diagnosis was made.

In March, 1957, the skin lesions reappeared and once again responded to Vioform ointment. There have been at least two recurrences since then. The last and current eruption persists despite the application of Vioform ointment, tars, resorcinol, hydrocortisone, etc., in various vehicles. No systemic medications have been administered. There have been no oral ulcers during the past year.

Upon examination now, one sees scattered over the body without predilection to any area nummular, gyrate, confluent, erythematous to salmon-colored patches, some well defined, others without definite borders. Several lesions are slightly infiltrated. Some of the patches are covered by a branny scale. There is a diffuse scaling of the scalp.

Discussion

DR. FRANCES PASCHER: I should like to suggest the diagnosis in this case of systemic reticuloendotheliosis (systemic reticuloendothelial hyperplasia [Wallgren], lipid granulomatosis, Hand-Schüller-Christian disease). One is obviously dealing with a systemic disease involving different organs with varying degrees of prominence at different times. The granulomatous infiltration of the intestine, hypersplenism, anemia and leukopenia, lung involvement, and oral lesions have all been described as manifestations of systemic reticuloendotheliosis. The lesions on the trunk and extremities, if seen in an adult, would be diagnosed I believe without hesitation as parapsoriasis en plaque (not guttate parapsoriasis) or mycosis fungoides in the premycotic phase. Mycosis fungoides is regarded by many observers as a form of reticuloendotheliosis. A picture like seborrheic dermatitis as seen on this patient's scalp has been described before as a symptom of reticuloendothelial hyperplasia. The hypo- or agammaglobulinemia may be a secondary manifestation, as in other malignant lymphomas. Roentgenographic examination of the bones may disclose evidence of eosinophilic granuloma. If found, this would then be important corroborative evidence for the diagnosis proposed.

DR. ALEXANDER A. FISHER: It is interesting that both agammaglobulinemia and reticulogranuloma have been considered in Dr. Witten's case. You may recall the follow-up report of congenital agammaglobulinemia in brothers which I presented at our meeting on April 21, 1957. This case was also considered a possible reticulogranuloma (histiocytosis). Eventually we established a diagnosis of agammaglobulinemia. Dr. Witten's case I believe is one of reticulogranuloma.

DR. FRANK KRASNER (by invitation): A biopsy was not performed, since it was feared that infection would occur at the biopsy site as gangrene had previously occurred at the site of a surgical cut-down on a vein.

The lesions, which at first responded to Vioform ointment and then failed to do so, have once again just begun to show signs of resolution with continued application of Vioform.

Diagnosis: Lymphoma. Presented by DR. A. J. ORFUSS.

A 68-year-old Negro has a history of gradual development of persistent and progressive severe itching of the face and chest for the past year. About three months after the onset of symptoms the patient noticed that the skin of his face and chest was turning darker in color.

The patient's general health has remained good. He takes "666 Cold Preparation" and "liver pills" on occasion.

On examination, the patient is well nourished and does not appear ill. The skin lesions are limited to the head and chest and consist of confluent elevated lichenified dark papular plaques. This appearance is most marked on the forehead, periorbital areas, upper cheeks, temples, below the ears, and over the sternum. There is no lymphadenopathy, and neither liver nor spleen is palpable.

A biopsy was read by Dr. Charles Sims as leukemia cutis. A bone marrow study was interpreted as "normoblastic hyperplasia with no indication of leukemia infiltration." Blood cell counts have shown relative lymphocytosis.

Discussion

DR. ALEXANDER A. FISHER: Dr. Orfuss's case presents clinically a lichenified dermatitis of the face and neck, a picture such as one could get in ragweed dermatitis. As a matter of fact I recall one case of ragweed dermatitis in which a histologic diagnosis of lymphoma was made. This condition cleared with appropriate treatment and a true lymphoma never did develop. Occasionally neurodermatitis will give a histologic picture somewhat resembling that of lymphoma.

DR. FRANCES PASCHER: There are significant changes in this patient's hemogram. A relative lymphocytosis ranging from 59% to 69% has been a consistent finding. This shift in the differential count is not sufficient to warrant a diagnosis of chronic lymphatic leukemia but may be interpreted as a leukemoid reaction of the lymphatic type to

a malignant lymphoma. The hematologic findings together with the monomorphous infiltration of lymphocytes, many of which are large and pale-staining, in the upper cutis support the diagnosis of lymphoma rather than contact dermatitis.

DR. CHARLES WOLF: The lesions strongly suggest that mycosis fungoides is in development.

DR. A. J. ORFUSS: In establishing this diagnosis I was impressed with the uniformity of the cellular infiltration together with the variation in the size of the individual cells. I feel that this diagnosis is a very likely one. I also feel that the prognosis in this case is good. The patient is a 68-year-old active Pullman porter without constitutional symptoms or signs. I do not feel that his health or life will be impaired in any way by this lesion. Sensitivity tests for pollen and other oleoresins will be carried out as recommended.

Diagnosis: Folliculites Depilantes des Parties Glabres (Arnozan); Folliculitis Sycosiformis Atrophicans Cutis Lanuginosa Corporis (Hoffmann). Presented by DR. FRANCES PASCHER and DR. CARLOS GAY (by invitation).

A 30-year-old man was first seen nearly 10 years ago with an eruption involving the bearded area. A diagnosis of folliculitis barbae was made. When seen again seven years later the patient gave a history of a recurrent eruption of the same sort over the years which got worse in the summer. Each episode lasted several months and became progressively more troublesome. The patient then migrated to Miami and was treated there by several dermatologists by means of salves, antibiotics, and corticosteroids, with but temporary improvement.

In October of this year, the patient returned to our observation with a widespread pustular eruption in follicular location on chest, upper back, arms, abdomen, and thighs. Areas of alopecia with follicular atrophy were also found.

Because of the patient's statement that his condition was worse in the summer and under his working conditions, sweat studies were done which revealed anhidrosis of the involved areas and heavy normal sweating of the unaffected areas.

A biopsy of the right forearm was read by Dr. Morrill as follows: There is folliculitis with marked focal inflammatory reaction made up of lymphocytes and plasma cells and a fibrotic reaction in the dermis. Sweat glands are present and are apparently normal except for the fact that they are embedded in a thickened and sclerotic dermis. The sebaceous glands appear to have been destroyed.

A second biopsy, this time from an area showing follicular atrophy on the right knee, was read by Dr. Sims as follows: The epidermis is somewhat irregular, with small foci of atrophy. The horny layer presents a loosely laminated configuration. The superficial vessels are mildly dilated and are surrounded by a sparse nonspecific reaction. The sweat glands are normal.

Culture of affected hairs showed coagulase-positive Staphylococcus pyogenes var. aureus which was sensitive to Chloromycetin, erythromycin, bacitracin, and Gantrisin and but mildly sensitive to streptomycin and sulfadiazine.

One month ago treatment was started with erythromycin (0.5 gm. four times a day) and Gantrisin (0.5 gm. four times a day). A week later the improvement was striking. Erythromycin was reduced to 250 mg. four times a day, and improvement has continued.

Discussion

DR. FRANZ HERRMANN: In response to sweat stimulation by our standard exposure to dry heat, sweating was practically absent in all skin areas in which lesions were visible, although all other areas showed distinct hyperhidrosis. We do not know the reason for the anhidrosis in the clinically affected areas. There is no microscopic evidence of any form of poral closure and of consequent glandular inactivation, nor are there any microscopic signs of sweat retention. Another histologic finding, however, may be pertinent for this deficiency of sensible sweating, namely, the fact that sebaceous glands are absent in the diseased areas. In the absence of sebum, the scaly skin surface may well adsorb the sweat with so great an avidity that a formation of droplets does not occur. This would be analogous to our observation that when water or sweat is dropped onto the surface of ether-extracted postmortem skin the drops are absorbed immediately, as water drops are taken up by blotting paper. Thus, a situation of *pseudo-anhidrosis* would arise in which the sweat delivered to the surface can evaporate and thereby can—just like insensible perspiration—sustain its natural function of promoting heat dissipation, while at no time manifesting itself in the form of sensible sweating.

DR. ABRAHAM J. ORFUSS: I should like to offer the diagnosis of follicular lichen planus or lichen planopilaris in this case. The lichenoid lesions, the follicular distribution, and the atrophy all serve to suggest this diagnosis for consideration.

DR. FRANCES PASCHER: An explanation is perhaps in order for the cumbersome terminology used to designate this case. We had the choice of using the French term introduced by Arnozan in 1892 or the Latin term suggested a few years later by Hoffman ("Handbuch der Haut- und Geschlechtskrankheiten," Vol. 13, Berlin, Springer-Verlag, 1932, p. 372) or of coining a new appellation, like epilating pustular folliculitis of the glabrous skin. Folliculitis decalvans is inappropriate because the

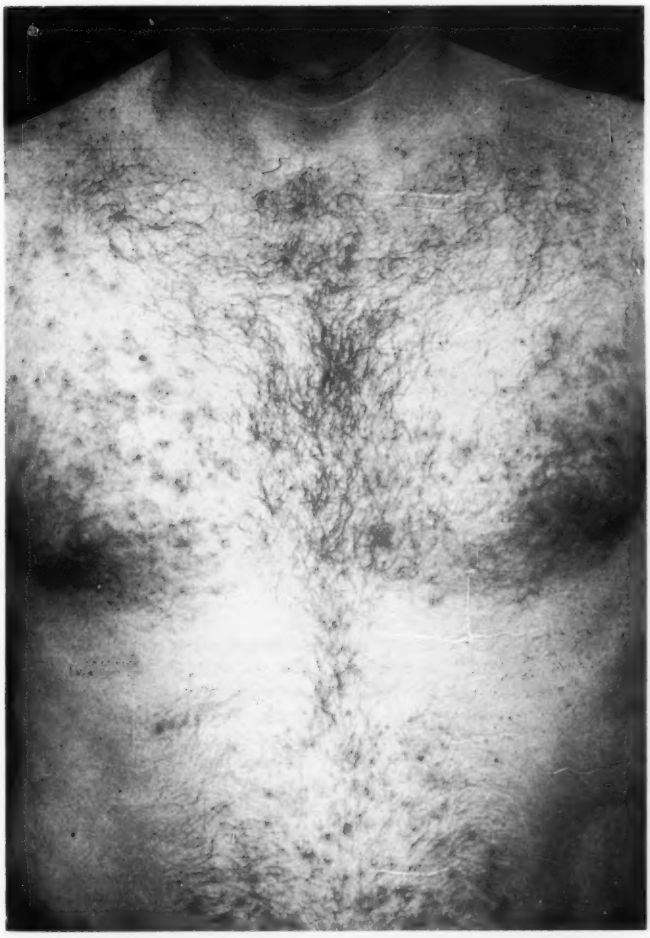


Fig. 1. — Miliary follicular pustules distributed around the hairs of the glabrous skin.

scalp is always affected in the latter, and in rare instances (according to Quinquaud's original description) the pubic and axillary hairs may be involved. In the case presented tonight the scalp was spared till recently, and the hair of the trunk and extremities rather than the pubic and axillary hair is involved.

I do not think that we are dealing with a varioliform infection. Although acne varioliformis may in rare instances affect the extremities, it would be most unusual for the face to be spared. The pustules in this case are not umbilicated. The scars, furthermore, are not varioliform. They are uniform, small, follicular, and punctate, giving the skin a sieve-like appearance. Although some eosinophils were noted in the cutis, we were more impressed with the infiltration of plasma cells, particularly about the follicles. The histologic as well as the clinical findings are identical with those described in the "Handbuch" for this rare form of folliculitis.

Follicular spines were noted when the pustules receded after the administration of Gantrisin and erythromycin. The spines are such as one sees in lichen spinulosus rather than in lichen planopilaris. No evidence of lichen planus was found histologically. The association of lichen spinulosus with this rare epilating folliculitis has been noted by others and has been reported by Traub, Senear, and Graham-Little.

Would the chairman be good enough to extend the courtesy of the floor to Dr. Gay, who contributed a great deal to the study of this case.

DR. CARLOS GAY (by invitation): We present this case because this condition is seldom mentioned in the English literature. In fact we could

find only one article, namely, that of Dr. Pardo-Castello (Dermatology in a Tropical Rural Zone, A. M. A. ARCH DERMAT. 74:115 [Aug.] 1956), in which 34 cases resembling mine are discussed under the title folliculitis decalvans. Since folliculitis decalvans is generally associated with the scalp, we bring to attention the title folliculitis sycosiformis atrophicans cutis lanuginosa corporis as more descriptive of a generalized condition perhaps of the same pathomechanism.

Case for Diagnosis: Furfuraceous Impetigo? Presented by DR. ALEXANDER A. FISHER for therapeutic suggestions.

An 8-year-old boy has had the present condition for about nine months.

There are several dry, scaly, slightly depigmented, circular patches on the face.

Also, there has been on occasion some scaliness of the ear canals. The lesions have not responded well to antibiotic and ammoniated mercury ointments.

Discussion

DR. ALEXANDER A. FISHER: I am presenting this case not only for therapeutic suggestions but also in order to elicit opinions on the classification of this condition. Does it belong with seborrheic dermatitis or with psoriasis? Is it due to a pyogenic infection? The eruption yields temporarily to various ointments, but we have not been able to obtain a lasting cure.

DR. MORRIS LEIDER: I offer the suggestion that this condition is a forme fruste of atopic dermatitis. This accounts perhaps for temporary improvement and ready relapse. I suggest the use of hydrocortisone ointment plus an antibiotic like neomycin in prolonged application.

DR. ABRAHAM J. ORFUSS: The pyogenic etiology of this condition has been pretty well exploded. This is not an impetigo. The organisms are ubiquitous ones living on the skin, producing no reaction whatsoever. I feel that this term should be dropped. My own impression is that we are dealing with an exaggerated chapping reaction or a form of atopic dermatitis.

DR. CONRAD STRITZLER: These eruptions are furfuraceous but are certainly not impetiginous. Gram stains of scrapings show organisms, usually micrococci, but few are no cells other than epidermal cells. These organisms evidently find these lesions to be good breeding grounds, but I do not believe that they cause the disease. I would suggest a diagnosis of a forme fruste of seborrheic dermatitis and would recommend the use of Abramowitz's paste of 40% ppt. sulfur in petrolatum for therapy.

DR. FRANCES PASCHER: This is a case of "form frustration." I saw this patient in my office a few months ago. I, too, prescribed ammoniated mercury, without benefit.

Diagnosis: Cylindroma (Turban Tumor, Sweat Gland Adenoma). Presented by DR. ALEXANDER A. FISHER.

A 58-year-old woman first noticed scalp and face lesions when she was about 20 years old. Eighteen years ago the very first tumor that appeared on her scalp was removed; it recurred, was removed again, and recurred again.

Upon examination now, there are scattered throughout the scalp and forehead at least 80 lesions varying in size from that of a small papule to that of a plum. The tumors are firm and reddish in color, and they show many dilated vessels on the surface. On the upper portion of the face

Fig. 2.—Cylindromas.

and nose are numerous small, flesh-colored and slightly red, firm nodules.

The histologic report of a large lesion removed from the scalp was as follows: "There is thin epidermis, and a narrow band of connective tissue separates it from the main mass in the cutis. The latter is occupied by closely set, very well defined islets of epithelial cells, which in many areas show distinct tubule formation. The stroma in relation to many is hyalinized. There is fibroblastic reaction, but only mild inflammation." Diagnosis: "Cylindroma, sweat gland adenoma."

A daughter is said to have had a similar eruption, which began at the age of 27 during her first pregnancy.

Aside from general interest, this case is presented for therapeutic suggestions.

Discussion

DR. HELEN O. CURTH: There are some additional genetic data on this family: The patient and the daughter have large and small tumors. The patient's father and his mother had small tumors. A sister of the patient and her children are not affected. A 37-year-old son of the patient is not affected. In view of the age at which his sister and mother developed the tumors, one is justified in assuming that the son may remain unaffected. The four children of the affected daughter are not yet affected, but since they range in age from 6 months to 15 years they are still likely to show the disorder at a later date. The involvement in this family indicates dominant inheritance with strong penetrance. The same pattern has been seen in other instances of the disorder.

DR. JOHN GARB: Turban tumor (cylindroma) is frequently associated with epithelioma adenoides cysticum. Biberstein (*Arch. Dermat. u. Syph.* 142: 428, 1923) reported a case of cylindroma on the scalp and epithelioma adenoides cysticum on the face. The tumors may occur on other parts of the body. A hereditary factor has been observed in many cases through several generations. Wiedmann (*Arch. Dermat. u. Syph.* 159:180, 1934) described the lesions in four generations of one family. Graul (*Dermat. Wchnschr.* 128:949, 1953) reported the occurrence of turban tumors in father and daughter, the latter showing also epithelioma adenoides cysticum. The percentage of occurrence in women is about twice that of men, in reports of 37 cases. The disease is a simple Mendelian dominant stronger in the female sex (Evans, C. D.: *Brit. J. Dermat.* 66:434, 1954). Cylindromas are considered by some authors to be nevoid in origin. Their growth is slow, and their behavior, generally benign, although some lesions grow as basal-cell carcinomas (Sutton and Sutton, "Diseases of the Skin," Ed. 7, St. Louis, The C. V. Mosby Company, St. Louis, 1956, 116). Evans performed experiments on mice with the extract of the lesions. They did not develop any tumors but showed premalignant changes.

The growths, especially the large disfiguring tumors, may be removed by bipolar electosurgery. The lesions on the face may also be removed by this method or by dermabrasion. However, plastic surgery of the cylindroma of the scalp should be strongly considered. Two such cases reported by Evans (*Brit. J. Dermat.* 66:435-439, 1953) are described. The tumor-bearing areas of the scalp were removed, and this procedure was followed by Thiersch grafting. Though the patients had to wear wigs they were pleased with the result, and their mental outlook improved considerably. One of the patients was able to obtain employment for the first time in many years.

Diagnosis: (1) Toxic Dermatitis Due to Pregnancy; (2) Impetigo Herpetiformis. Presented by DR. EDWARD H. MANDEL and DR. IRWIN I. LUBOWE.

A 21-year-old Puerto Rican woman, now in the seventh month of pregnancy and having already borne two children, complains of itching and burning of the breasts, abdomen, back, thighs, arms, and legs of three weeks' duration. Three weeks previous to admission to the hospital she complained of chills, fever, and pruritus subsequent to the appearance of the rash. In her previous pregnancies, four years and two years ago, there was no evidence of a similar rash.

To examination there is a confluent erythematous scaly dermatitis involving the nipples, umbilicus, and sides of the abdomen, back, and thighs. Originally these erythematous areas were studded with discrete vesicles, pustules, and crusts. The pruritus is extreme.

Biopsy was interpreted by Dr. Sala as impetigo herpetiformis.

Treatment has consisted of oral administration of Gantrisin (1 gm. q. i. d.), Meticorten (30 mg. daily), Chlor-Trimeton (8 mg. t. i. d.); intravenous administration of calcium gluconate (10 gm. b. i. d), and topical application of Bacitracin ointment. There has been some improvement.

Discussion

DR. PAUL GROSS: On the basis of the colored photographs which were presented with the patient, the clinical picture fits well with what is known as impetigo herpetiformis. In making this diagnosis we should be aware of the fact that there is fairly wide agreement, especially among European dermatologists, that impetigo herpetiformis is a

form of psoriasis. On the other hand, this is not true of acrodermatitis continua of Hallopeau, which also has been considered by some to be identical with pustular psoriasis.

Diagnosis: Pigmented Basal-Cell Epithelioma of the Back. Presented by DR. MAX WOLF.

Diagnosis: Chronic Lymphedema. Presented by DR. ABRAHAM J. ORFUSS.

Diagnosis: Lymphoblastoma Cutis with Involvement of Paratracheal Lymph Nodes. Presented by DR. CONRAD STRITZLER.

Diagnosis: Lichen Spinulosus. Presented by DR. ERNST M. ROSENBAUM.

BRONX DERMATOLOGICAL SOCIETY

Jan. 16, 1958

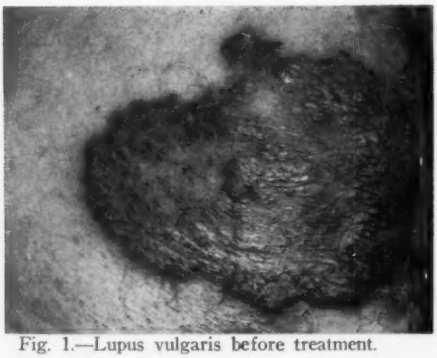


Fig. 1.—Lupus vulgaris before treatment.

Lupus Vulgaris of the Left Buttock. Presented by DR. MAX WOLF.

A white man now 68 years of age was found to have tuberculosis of the left ankle joint in 1946. Amputation of the left leg, 7 in. below the left knee, was performed in 1947, after unsuccessful ankle fusion. In the same year a cold abscess was excised, and two years later surgical fusion of the lumbar vertebrae was performed because of tuberculosis in the region.

The present skin condition appeared about one year ago and developed into a violaceous well-defined patch that measured about 5×4 in. and covered most of the left buttock. The center of the patch was crusted and boggy. The peripheral zone (1 in. wide) was raised above the level of the surrounding normal skin and consisted of closely set or confluent soft papules. A probe could be sunk into the papules with moderate pressure, demonstrating the "apple jelly" character of these lesions.

A biopsy specimen was interpreted by Dr. A. B. Hyman as "verrucous lupus vulgaris with resemblance to tuberculosis verrucosa cutis."

Treatment consisted of oral administration of Rimifon in doses of 50 mg. three times daily for one month and 50 mg. daily for three more months.

Received for publication Feb. 26, 1958.

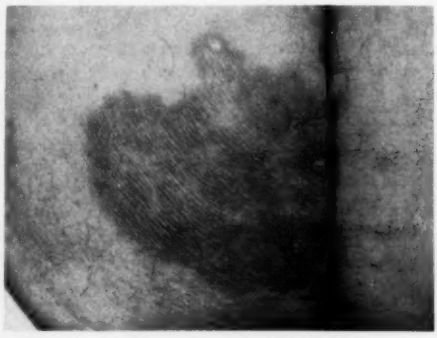
The improvement can be seen clinically and from the photographs (Figs. 1 & 2). The area of involvement is flat and consists merely of brown-red discoloration.

Discussion

DR. MORRIS LEIDER: The result seen in this case is, I believe, the universal experience with isoniazid therapy of bacillary-laden cutaneous tuberculosis. Not only lupus vulgaris but all other tuberculoderms that contain living tubercle bacilli, like tuberculosis cutis verrucosa, tuberculosis cutis colliquativa (scrofuloderma), tuberculosis cutis indurativa (Bazin's disease, erythema induratum), and the primary complex of tuberculosis, respond quickly to isoniazids. Cases that have been progressive for decades yield to the treatment. Ideally tuberculosis should be eliminated by bacterial sanitation of the world, but, failing this, drugs of the class of isoniazids are a boon for cutaneous tuberculosis at least.

DR. FRANCIS PASCHER: Optic neuritis and atrophy as well as peripheral neuritis are known complications of isoniazid therapy. These side-effects have occurred in patients treated with large doses of the drug for visceral tuberculosis. Pyridoxine has been recommended as a prophylactic and therapeutic measure and should be used rou-

Fig. 2.—Lupus vulgaris five months after treatment.



tinely in conjunction with isoniazid in an approximate ratio of 25 mg. of pyridoxine to 50 mg. of isoniazid.

DR. DAVID BLOOM: Patients treated for visceral tuberculosis not infrequently develop generalized eruptions. As they are usually treated with a combination of aminosalicylic acid, streptomycin, and isoniazid, we advise the omission of one drug at a time to find out what drug produces the eruption. I have never seen an eruption caused by isoniazid, and if this drug produces untoward cutaneous reactions the event must be rare. Streptomycin and aminosalicylic acid are known to produce eruptions.

DR. MAX WOLF: Lupus vulgaris may appear at advanced ages, particularly in association with bone tuberculosis.

I am informed by Prof. Dr. G. Riehl that at the Lupusheilstätte in Vienna the practice is to give 50 mg. of isoniazid per 10 kg. of body weight to a total of 1500 mg. in every case of lupus vulgaris. The theory is that this amount is necessary for prevention of recurrence. My case has not had this amount, and I am considering continuation of treatment in view of the underlying bone tuberculosis.

Generalized Vascular Nevoid Disturbance. Presented by DR. JOHN GARB.

A 26-year-old man presents a generalized skin disturbance present since birth.

There is no consanguinity in parents and grandparents and no similar disturbance in other members of the family. The patient is said to have had some injury at birth resulting in a permanent shortening of the left arm and "spells" until 12 years of age. The lesions have never changed in extent and appearance.

The lesions consist of purplish-red macules that are discrete and irregular, varying in size from that of a pea to that of a half-dollar. The color is more intense on the neck. The face is smooth and purplish-red; the ears, somewhat darker.

A crusted patch on the right forehead which had been present for five years was destroyed a year ago, recurred, and was again destroyed in October, 1957. On the dorsa of hands are well-defined patches, split pea- to dime-size, with the appearance of yellow plastic adhesive imbedded in the skin. Diascopic pressure on the lesions on chest and shoulders obliterates the erythema and reveals telangiectatic vessels underneath.

There is slight ptosis of the left upper eyelid. The pupils, nails, teeth, and oral mucosa are normal. The left upper extremity is about 1 in. shorter than the right, but it appears to be otherwise normal.

Histologic examination of a patch of the left shoulder and dorsum of left hand suggests a nevoid vascular disturbance. Histologic report of a crusted and thickened patch on the right forehead was read as keratosis with Bowenoid changes.

Discussion

DR. ABRAHAM J. ORFUSS: My impression of this case is that it is a forme fruste of a systemic angiomatosis of the Sturge-Weber type. He has symptoms and signs that are suggestive of this condition, namely, epileptiform seizures, varying length and size of the extremities, and the angiomatous lesions of the skin.

DR. JOHN GARB: I have not thus far found any case in the literature that is comparable to that of this patient. F. Parkes Weber ("Rare Diseases and Some Debatable Subjects," London, Staples Press, Ltd., 1947, p. 9.) describes Sturge-Kalischer disease, and my first thought was that my patient has this syndrome. However, patients with Sturge-Kalischer disease have associated cerebral lesions, usually on the same side as the cutaneous angiomas; neurologic manifestations such as convulsions and paralyses, and mental retardation. Ocular abnormalities consisting of unilateral exophthalmos associated with blurred or double vision, blindness, ocular palsies, and congenital glaucoma are frequently present.

A photograph of the patient of Dr. Parkes Weber on page 9 of the above-mentioned book illustrates a typical case of Sturge-Kalischer disease. My patient gives a history of a birth injury and epileptiform convulsions in his youth. There is mental retardation, but neurologic and electroencephalographic findings are normal. Also, the cutaneous lesions are telangiectatic and do not have the appearance of portwine marks as seen in the typical Sturge-Kalischer disease. It is possible that my patient may have a forme fruste of this syndrome.

Ichthyosis Treated with 10% Sodium Chloride Ointment. Presented by DR. ABRAHAM J. ORFUSS.

A 6-year-old girl presented dryness and scaling of the skin since birth in the typical character of ichthyosis vulgaris of moderately severe grade.

At the suggestion of Dr. Hyman Gordon, an ointment of 10% sodium chloride was applied to the back. The improvement was so good and immediate that inunction of all affected areas was ordered. Equal improvement occurred everywhere except on the scalp. During the treatment, controls with the hydrophilic and plain petrolatum vehicles were seen to be inferior to the preparation containing sodium chloride.

Discussion

DR. EDWARD H. MANDEL: After a discussion with Dr. Franz Herrmann, I treated a patient with ichthyosis by exposure to a heat cradle just long enough to induce the flow of sweat. The heat cradle was then removed, and the sweat was permitted to evaporate. The patient was treated two times a week for one month. Significant improvement was noticed from this procedure alone.

DR. JOHN GARB: Sodium chloride is known to have a good effect on other diseases, namely, psoriasis of the scalp. Saline baths ought, of course, be a good adjunct to treatment of conditions like ichthyosis.

DR. HELEN O. CURTH: I also have been gratified by the results of sodium chloride topically. One great advantage of this treatment is the avoidance of preparations containing salicylic acid, which may become toxic since they are given for a long time and over wide areas of the body. I wonder, though, if the effect of sodium chloride preparations is related to what happens with adequate sweating. Ljungstrom (Ljungstrom, C. E.: Eine einfache und wirksame Therapie bei Ichthyosis, *Acta med. scandinav.* 108:98-105, 1941) conceived this theory in a rather naive way and did not base it on experiments. The effect of sodium chloride on ichthyotic skin may be specific or based on a specific principle.

I also want to call your attention to the fact that this child's skin condition, which, we agree, is ichthyosis simplex, a variant of ichthyosis vulgaris, was present at birth. The fact that ichthyosis vulgaris may be present at birth is not surprising since, such variations of onset of a disorder are common in a genodermatosis. However, the belief that ichthyosis vulgaris is never present at birth has, unfortunately, been deeply entrenched in the minds of the dermatologists. Although there were no signs of erythroderma but definite signs of ichthyosis vulgaris present in several members of a family-group, Floden (Sjögren, T., and Larsson, T.: Oligophrenia in Combination with Congenital Ichthyosis and Spastic Disorders: A Clinical and Genetic Study, *Acta psychiat. et neurol. scandinav.*, Supp. 113, Vol. 32, 1957) defends the diagnosis of ichthyosiform erythroderma, a variant of ichthyosis congenita, by stating that "the ichthyosis was congenital and the disease was stationary throughout life, from which it is clear that it cannot have been ichthyosis vulgaris." I suggest that for a while, whenever we see ichthyosis vulgaris at birth, we emphasize such an occurrence until the possibility of cutaneous lesions at birth in ichthyosis vulgaris has become common knowledge.

DR. SAMUEL B. FRANK: This presentation calls to mind an observation I made some time ago. In a baby who had a severe ichthyosis I observed that the diaper-area skin appeared much less ichthyotic. Thinking that perhaps this improvement was produced by urine, I advised the mother to wrap one leg with a urine-soaked diaper once daily. When seen the following week the treated leg showed definite improvement. It is possible that the sodium chloride in the urine might have been responsible for the favorable effect.

DR. FRANZ HERRMANN: It is to be expected that further trials will substantiate Ljungstrom's early report and Dr. Gordon's present results in that NaCl incorporated in high concentration in water or ointment is beneficial to ichthyotic skin, whereas water or ointment alone fails to produce a similar effect. I would regard an increase in the transepidermal water supply of the stratum corneum and a consequent increase in the hydration of its base ("barrier zone") as responsible for that beneficial influence.

Multiple Myeloma, with Cutaneous Manifestations Simulating Lymphoma Cutis. Presented by DR. CONRAD STRITZLER.

A 65-year-old man presents a seborrheic dermatitis-like eruption on the face, edema of the eyelids, a generalized, infiltrated papular, and nodular eruption on the trunk and extremities, and edema of the penis and ankles.

About two years ago, he had a severe zoster involving the left thigh and leg, and following this he noted some numbness of the left leg and foot. The eruption on the face and body did not appear until about five months ago. The patient's only complaints are the numbness of both legs and feet and the eruption on the face and trunk. There was no pain until recently, when he suddenly developed pain in his right leg, in addition to numbness. He has continued at his occupation as a lumber salesman and drives a car with no difficulty.

When first seen the eruption on the trunk consisted of innumerable, small, closely set, pinkish to skin-colored infiltrated papules, about the size of a pea. During the past two months many of these papules have been absorbed, but new nodules appeared, chiefly scattered on the trunk, purplish-pink in color, and varying in size from that of a hazel-nut to a walnut. Now, these nodules are disappearing.

The lymph nodes of the neck, axillae, and groin are enlarged. There is hepatosplenomegaly. Edema of the eyelids, penis, and ankles has persisted.

Hemogram and urinalysis are within normal limits. Bleeding and coagulation time and platelet count are normal. Total proteins are 6.92 gm., with a ratio of albumin to globulin within normal limits. Electrophoretic studies on blood show an abnormal globulin ("myeloma globulin") adjacent

to the γ-globulin peak. The urine failed to show Bence Jones protein by chemical analysis but showed a definite trace of "myeloma globulin" on electrophoresis. Bone marrow smear showed from 10% to 17% "myeloma cells" (abnormal plasma cells). The rest of the smear was within normal limits. Biopsy of a nodule from the thigh showed relatively normal epidermis and a clear zone (grenz zone) separating the basal cells from a fairly dense infiltrate in the cutis, consisting of lymphocytes, histiocytes, and a number of huge giant cells. Neither plasma cells or amyloid was found.

Therapy has consisted of Meticorten, 5 mg. q. i. d. Urethan plus steroid therapy is contemplated later if the clinical condition warrants it.

Discussion

DR. FRANCES PASCHER: We are all beholden to Dr. Stritzler for presenting this instructive case. One reads about the cutaneous manifestations of this disease, but one rarely has an opportunity to see an example. As in the leukemias and the lymphomas one may see specific lesions, due to the infiltration of the cutis with abnormal cells, which in this instance are plasmocytomas. Nonspecific lesions attributable to the associated dysproteinemia may also occur, e. g., purpura related to cryoglobulinemia or macroglossia related to amyloidosis. The facies in this case closely resembles that of dermatomyositis, and the lesions of the body are indistinguishable clinically from the specific lesions one may see in Hodgkin's disease or lymphatic leukemia. The differential diagnosis rests on a more detailed examination. The normal A/G ratio is particularly noteworthy, making it plain that a quantitative determination alone is not sufficient but that qualitative studies, i. e., patterns determined by electrophoresis, must be part of the study.

DR. CONRAD STRITZLER: This is one of the most fascinating cases I've ever seen. It is a veritable maze of dermatological, internal medical, and hematological problems. A few points are worthy of reemphasis. 1. The edema about the eyes and the seborrheic dermatitis-like appearance of the face occurs fairly frequently in multiple myeloma, though it cannot be considered pathognomonic. This point has been emphasized by Bluefarb. This patient is a striking example of this cutaneous reaction. 2. The total protein and A/G ratio which are "normal" emphasize the importance of electrophoretic studies which reveal abnormality. Wintrobe states that the total protein may be within normal limits in 35%-50% of cases, but 75% of cases show abnormal electrophoretic patterns. 3. The importance of bone marrow studies is self-evident. 4. The cutaneous reaction with the huge giant cells, suggest a reaction to a foreign protein, possible the "myeloma globulin," deposited in the cutis. An effort will be made to study this by histochemical techniques.

Pemphigus Erythematosus (Senear-Usher Syndrome). Presented by DR. H. MANDEL.

A 35-year-old white man was apparently well until three months ago when he developed an "irritation" on his nose. This was treated with cortisone ointments, wet dressings, and other agents, all to no avail. One month ago vesicular lesions that resembled the exanthem of chickenpox appeared. Itching and aggravation by sweating were complained of. At present the eruption is extensive in the "seborrheic" regions. The scalp, cheeks, nose, chest, and back show exudation and heavy crusting.

Biopsy confirms the clinical diagnosis of Senear-Usher syndrome.

Treatment has been just begun with intramuscular injections of 80 units of ACTH gel daily and 48 mg. of Medrol, 75 mg. of Pathilon, 20 mg. of Nilevar, and 1 gm. of potassium chloride by mouth daily. If the patient does not respond rapidly, it is planned to hospitalize him for intravenous ACTH therapy. Further therapeutic suggestions are invited.

Discussion

DR. FRANCES PASCHER: The heroic measures already instituted in this case are, in my opinion, unwarranted. One must bear in mind that patients with this particular form of pemphigus may live and function, despite the disease, for 20 years or longer. The treatment risks taken must not be disproportionate. Moreover, it has been my experience, and I believe this coincides with the experience of others, that Senear-Usher pemphigus is rather refactory to corticosteroid therapy. Since the presenter requests therapeutic suggestions, I should like to propose Aralen phosphate, 250 mg. two or three times daily. I have not had an opportunity to use this drug in this condition, but it seems plausible to do so in view of the lupus erythematosus-like lesions. If used, it should not be given in combination with massive doses of corticosteroids because its value could not then be told.

DR. DAVID BLOOM: In my experience, which may not be too great, Senear-Usher type of pemphigus does not require larger doses of steroids for control but rather less than pemphigus vulgaris. As to this patient, I believe that the administration of so many drugs is unwise. I would prefer also to omit ACTH entirely and give steroids only in the form of prednisone or prednisolone, as the latter do not usually cause retention of sodium chloride and excessive excretion of potassium and do not influence the blood pressure.

DR. MAX WOLF: Some cases of Senear-Usher syndrome undergo a rather sudden change from a mild course to the more severe picture of pemphigus vulgaris. The question arises whether we are able to prevent the outbreak of pemphigus vulgaris in the future by administering higher dosages of steroids from the very beginning of the treatment.

DR. CONRAD STRITZLER: The use of anabolic agents to prevent osteoporosis and subsequent compression spine fractures is warranted, I believe, especially when long-term therapy is necessary in the elderly. Once these changes occur they are practically irreversible, and, surely, it is good preventive medicine to attemp to forestall such complications. Whether such measures actually do prevent these sequelae in a sufficient number of patients, is, I believe, not definitely known and should be subjected to properly controlled clinical studies.

DR. SAMUEL B. FRANK: I would appreciate it if any one can tell me if there is any proven evidence from actual experience that the use of antiulcer therapy acts as a reliable prophylaxis against ulcer formation in patients given prolonged steroid therapy.

DR. MORRIS LEIDER: I, too, am in agreement with those who have said that the therapy instituted in this case is too heroic and too polypragmatic. It is true that pemphigus is a frightening disease, but rarely is it so fulminating in course that its control must be instantaneous. I wonder if the serious and frequently fatal complications of therapy by ACTH and adrenocorticosteroids that were so common a few years ago were not caused by the practice of starting with very high initial doses. It seems to me safer to start with moderate doses and then rise to higher ones if necessary. Is it not a guess as to what will control, and should one not guess conservatively?

DR. EDWARD H. MANDEL: Pathilon is an anticholinergic drug and is used in the management of gastric ulcers. Nilevar is used to convert a negative nitrogen balance to a positive balance. In view of the possibility of lifelong steroid therapy, it was felt that these medications should be used prophylactically to protect the patient from the potential complications. Aralen has already been ordered for the patient. He will take 1 tablet a day.

I am unable to agree with the theory of therapy by moderate dosage. This is not in accord with the literature or with my training.

I was happy to hear of the good prognosis of the patients of Dr. Bloom. I am certain the family and the patient will also be gratified. Unfortunately, I feel that the prognosis is graver in this type of pemphigus than in pemphigus vulgaris.

Case for Diagnosis: Angioma; Angiokeratoma?

Presented by DR. ERNST M. ROSENBAUM and (by invitation) DR. P. VAN BOCKSTAELE.

A 39-year-old Negro woman presents on both labia majora numerous pinhead- to somewhat larger-sized papules. They are scattered over the labia and are of reddish or purplish color.

Their duration is said to be about one year.

There is no itching or pain in the lesions. The papules resemble angiokeratomata of the scrotum as described by Fordyce and Sutton. There are no other lesions on the genital area or on any other part of the body.

Biopsy report (Dr. Sims): "The subepidermal corium presents thin walled vessels, varying in size and shape, with some containing red blood cells and some fibrin. The surrounding corium presents scattered fibroblasts. The epidermis is irregular with thinning in part. Diagnosis: Angioma."

Discussion

DR. DAVID BLOOM: After having read some of the literature on the subject of angiokeratoma, I favor the following classification: A. Angiokeratoma Mibelli, located on toes and fingers, based on and associated with perniosis, is a hereditary dermatosis with dominant mechanism. B. Angiokeratoma corporis diffusum, studied in recent years particularly by Ruiter (*A. M. A. Arch. Dermat. & Syph.* 68:21, [July] 1953; *Dermatologica* 109: 273, 1954), is a recessive hereditary condition, based on a lipoid metabolic disturbance involving the blood vessels of the viscera and the skin and leading frequently to death by uremia in young persons. C. Angiokeratoma scroti (or vulvae) is to be considered a nevus related to senile angiomata. This latter opinion was expressed by Wertheim ("Handbuch der Haut- und Geschlechtskrankheiten," edited by J. Jadassohn, Vol. 12, Pt. 2, Berlin, Springer-Verlag, 1932, p. 415).

DR. ARTHUR B. HYMAN: Angiokeratomas of the vulva are not uncommon, and, of course, correspond to the commoner angiokeratomas of the scrotum described by Fordyce. The keratotic element is rather unimportant; the angiomatous element consists of very dilated capillaries in the papillae, which if enclosed may seem to be within the epidermis. Their only significance is that they are liable to bleed, particularly while the patient is bathing, and may frighten the patient. Desiccation of the lesions is all that is needed to cure them. New lesions are likely to develop.

Case for Diagnosis: Dermatitis Herpetiformis. Presented by DR. ARTHUR B. HYMAN and DR. SAUL BLAU.

Case for Diagnosis: Sarcoid. Presented by DR. ANDREW G. FRANKS.

Case for Diagnosis: Multiple Cutaneous Leiomyomata. Presented by DR. ALFRED W. KOPF and DR. MARVIN ACKERMAN (by invitation).

Case for Diagnosis: Secondary Syphilis (Two Cases). Presented by DR. WILLIAM CURTH.

Case for Diagnosis: Lichen Planus of the Left Thigh Associated with Varicose Veins. Presented by DR. MAX WOLF.

Case for Diagnosis: Syphilitic Aneurysm of the Innominate and Right Subclavian Artery. Presented by DR. CONRAD STRITZLER.

THE CLEVELAND DERMATOLOGICAL SOCIETY

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Jan. 23, 1958

Lethal Midline Granuloma. Presented by DR. JEROME Z. LITT.

This is the first Crile Veterans' Administration Hospital admission for this 42-year-old yhite man, who is admitted with a history of stiff, sore neck for one month.

This patient was in good health until June, 1956, at which time he developed a "cold sore" in the back of his throat. This lesion was a small ulcer. Shortly after this he developed several similar lesions in the back of his throat, all of which were slightly painful to the touch. Following this the patient developed constant ache in the back of his mouth and also developed dysphagia, which has become progressively worse. The ulceration continued and he later developed the same type of painful "cold sore" in his right axilla and on his scrotum.

In October, 1956, the patient was admitted to University Hospital in Columbus, where a biopsy of the tissue of the throat and a node from the left axilla was performed.

The patient also had a bone marrow examination done and a histoplasmosis skin test, which was reported as positive.

While in the hospital he had a bout of pneumonia, which was treated successfully with penicillin. The penicillin therapy was continued for 24 days, and after this period the mouth lesions cleared somewhat and became much better and the dysphagia decreased.

Approximately three months prior to this admission to Crile Hospital the patient developed anorexia due to the painful swallowing. He also noticed at this time that there was erosion of the palate, with regurgitation of solids and liquids through the nose. Approximately two months prior to admission he developed a change in his voice, with a progressive nasal quality to it. He also noticed a stiff neck and bilateral swelling in the front of his neck. He developed a cough and swelling of his throat, which made it difficult to eat. He also became short of breath. The cough has been productive of mucoid and mucopurulent sputum. He has had a 40 lb. weight loss since March of this year.

Examination of the mouth revealed the mucous membranes to be dry. The tongue was coated with a brownish-white material and had a fuzzy appearance. The patient is completely edentulous. There is pallor to both the hard and the soft palate, with some marked bilateral erosion of the distal soft palate and some slight edema of the uvula. There is grayish-white thick membrane, rather tenacious and nonfriable, which is not caused to bleed by manipulation, visible in the posterior pharynx in the right tonsillar fossa. There is some evidence of chronic inflammation around this membrane, which extends below the visible level at the base of the tongue. The patient is unable to open his mouth to any great degree because of severe pain. Examination of the abdomen reveals that the left lobe of the liver is palpable 2 to 3 fingerbreadths below the right costal border. The liver is smooth and not irregular. The patient has a 1 cm.-sized, indurated, ulcerated type of lesion on the scrotum, at the base of the penis. There is no bleeding or pus from this lesion, and it is only slightly painful. He has palpable anterior cervical nodes, a postauricular node on the left, and several small, soft, T-shaped nodes in each axilla. He also has several small, slightly firm nodes in each inguinal region.

Laboratory studies: VDRL negative. Urinalysis normal. The white cell count was 14,500. Hemoglobin 11.55 gm. Total protein 6.8 gm., albumin 3.9 gm., globulin 2.9 gm., with a ratio of 1.3:1. A throat culture showed Staphylococcus aureus, viridans Streptococcus, and yeast cells.

A chest film showed an emphysematous chest, with bleb formation in both lung bases, especially on the left, and some prominence of the pulmonary outflow tract. The gastrointestinal series showed a probable filling defect in the midportion of the

Submitted for publication May 19, 1958.

lesser curvature of the stomach, which was interpreted as being a probable benign peptic ulcer. The barium enema was negative. A KUB film of the abdomen showed degenerative changes in the lumbar vertebrae, with a suggestion of narrowing at the L-3 and L-4 interspaces.

During his stay at Crile Hospital the patient had a biopsy of a cervical node and a biopsy of the mouth lesion on Sept. 11, 1957, which was interpreted as indicating chronic sialadentis of the submaxillary gland and chronic inflammation of the stratified squamous mucosa of the pharynx. There was no tumor.

On Oct. 1, 1957, a consultation was held with the ear, nose, and throat service, at which time he was noted to have much edema, hyperemia, and superficial ulceration of the oropharyngeal structures. On Oct. 10, 1957, he had direct laryngoscopy under 0.25% Pontocaine hydrochloride. His cords were well visualized and mobile. There was an edematous area on the right cord anteriorly, which was biopsied. There were also two areas of the biopsied ulcerative tissue from the pharynx which were submitted for tissue culture.

There has been gradual improvement in the lesion of the patient's oral pharynx, which is apparently responding to large doses of penicillin.

Discussion

JEROME Z. LITT, M.D.: This is a rather unusual condition; I have seen only one other. That one began on the right nostril and invaded the maxilla.

In the literature, I could find only six cases in the American and a few in the foreign literature of lethal midline granuloma. Some were considered to be allergic, and some, neoplastic. In every case death has resulted and at the autopsy no one has been able to determine the exact cause. It has been suggested, in view of the fact that it may be an allergic phenomenon, that corticosteroids be given. In some cases large doses of antibiotics have been tried, with constant progression of the process.

I should like to ask if you think that x-ray therapy might be of value and possibly the use of corticosteroids, and I should also like possible help in the diagnosis.

GEORGE BINKLEY, M.D.: Before we go into the question of how to treat the patient, I would like to ask whether there is any relation between this disease and von Wegener's granulomatosis.

JEROME Z. LITT, M.D.: Dr. Dorner asked me the same question. There are some people who believe that this condition has a single etiological factor. Others believe it is on an allergic basis, with subsequent granulomatosis.

GEORGE H. CURTIS, M.D.: I have been fortunate enough, or rather unfortunate enough, to have seen two cases of this disease at the Cleveland Clinic. The patients, of course, were admitted to our department of otolaryngology. Both were men. Although they were seen rather late in the course, with extensive involvement of the soft palate and nasopharynx, ionization therapy, including the cobalt bomb and high-voltage x-ray, with large doses of several antibiotics, were used and failed. Both patients died of the severe toxic effects of the disease.

Sarcoidosis. Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Case for Diagnosis: Mycosis Fungoides? Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Keratoderma Palmaris et Plantaris—with Destructive Lesion of the Right Palm. Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Case for Diagnosis: Folliculitis Decalvans; Pseudopelade (Brocq)? Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Case for Diagnosis: Lymphoblastoma? "Hodgkinid." Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Case for Diagnosis: Lichen Planus Linearis; Lichen Striatus; Linear Nevus? Presented by DR. MELVIN BRODY.

Case for Diagnosis: Acne Varioliformis; Neurotic Excoriations? Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Lupus Erythematosus (Chronic Discoid). Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Alopecia Areata (Following Trauma?). Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Thrombophlebitis with Lymphedema. Atopic Dermatitis. Presented by DR. IRVING L. SCHONBERG and DR. JEROME Z. LITT.

Rhinophyma. Presented by DR. IRVING L. SCHONBERG.

MANHATTAN DERMATOLOGICAL SOCIETY

Paul Gross, M.D., President

Maurice J. Costello, M.D., Secretary

Jan. 14, 1958

Case for Diagnosis: Poikiloderma of Civatte; Melanodermitis? Presented by DR. NATHAN SOBEL.

A 46-year-old Puerto Rican woman has had an eruption for the past four years. It began in a small area over the right jaw and gradually spread.

There is a markedly reticulated hyperpigmentation of the skin of the lower part of the right cheek, the entire right side of the neck, and part of the adjacent chest. Most of the rest of the face shows a diffuse hyperpigmentation without reticulation, which is also present over most of the medial aspect of the right forearm and a palm-sized area

Submitted for publication May 28, 1958.

on the external aspect of the right knee. Xerosis of the skin of the extremities is present.

A biopsy specimen taken from the right side of the neck about three years ago was reported as "pigmentary disturbance."

The patient was treated several years ago for a basal-cell epithelioma located on the bridge of the nose and shows the resultant scar with moderate radiodermatitis.

Discussion

DR. THOMAS N. GRAHAM: I would say it is an unusual case of poikiloderma of Civatte or melanodermatosis. The cause in this case, of course, is not known.

DR. JACK WOLF: Clinically, this eruption has none of the appearance of poikiloderma of Civatte. The eruption is one of melanoderma which will probably become more extensive, appear in other locations, and may ultimately involve internal organs and lead to the patient's death.

DR. A. C. CIPOLLARO: I agree with Dr. Wolf's remarks. I believe this is an example of melanoderma, rather than one of poikiloderma of Civatte. The latter is nearly always bilateral, and one of its most prominent features is telangiectasia, which is absent in this case.

DR. M. J. COSTELLO: I would prefer the term suggested by Dr. Machacek—melanodermitis—because some inflammatory process is associated with this condition. Dr. Sobel stated that telangiectasia was present. The eruption is on the front and sides of the neck, not on the back. I think it is on the basis of some chemical trauma because it is unilateral; there are some areas of inflammation, associated with hyperpigmentation. It is most difficult to improve this condition. Some here said it may be associated with internal malignancy. I had a patient like this one whom I presented before this society six or eight years ago, with an eruption not unlike this, although the pigmentation was more extensive, who later died of an internal cancer.

DR. JOHN W. DOUGHERTY: I don't know how far we could trust the patient's statement, but she says she sweats more on the side of the eruption. Anticholinergic drugs or a stellate ganglion block could be done.

DR. WILBERT SACHS: The light was so strong that I couldn't see any detail, but I did see pigment in the subepidermic region and a small amount of pigment in the basal-cell margin. I could only say there was inflammation with some type of pigmentation. I would not be inclined to believe that this was on a systemic basis, because then I would expect most of the pigment to be on an acanthotic basis and it is not. If you are talking about hemochromatosis, one would expect a lot more pigment. Most of the pigment here is right under the epidermis, and secondary to the inflammation.

DR. JACK WOLF: How can you tell this is not a systemic melanosis?

DR. WILBERT SACHS: If it were systemic, you wouldn't have inflammation in the dermis. Here, while there is a slight amount of pigment in the epithelium, you have a definite inflammation, and on that basis I thought it was postinflammatory.

DR. PAUL GROSS: The history of this patient may contribute to the diagnosis and the cause of her eruption. She is a machine operator and comes in contact with machine oil. This may explain the diffuse involvement of her right arm, which rests on the board of the sewing machine. Therefore, I favor the diagnosis of melanodermitis toxica (Erich Hoffman). As far as poikiloderma of Civatte is concerned, this is accepted as another name for melanodermitis, based on photosensitivity due to impurities in petroleum derivatives. Observations on these conditions in Central Europe during World War II are similar to those made during World War I. The tendency is to separate melanosis of Riehl from melanodermitis and to attribute it to nutritional deficiency. I believe that poikiloderma of the triangle of the neck, seen in menopausal women, should be separated from poikiloderma of Civatte and should be considered due to endocrine disturbances.

DR. DAVID BLOOM: As Dr. Costello has mentioned, this pigmentation does not differ in appearance from the pigmentation seen in dyskeratosis congenita. This fact, and the localized hyperhidrosis in the area of pigmentation on the left side of the neck and cheek, speak for an internal and not an external causation.

DR. NATHAN SOBEL: I just saw this patient for the first time two days ago, and so I didn't have time to do any extensive studies. Dr. Franz Herrmann is very much interested in the question of the sweating at the side of the neck and will make a special investigation of this. The patient also says she uses perfume, and this may be an additional cause of the pigmentation besides the oil she handles.

Case for Diagnosis: Nevus. Presented by DR. THOMAS N. GRAHAM.

A Puerto Rican girl, aged 13, was first seen by me at the New York Eye and Ear Infirmary on Jan. 3, 1958. Her father stated that she had had a bald spot on the right side of the scalp since birth and that it had been increasing in size and had become raised several years ago.

There is an area of partial alopecia approximately 2 cm. by 1.5 cm. on the right side of the scalp near the midline. The central area of the

lesion is elevated and papular, with a verrucous surface.

A biopsy has not yet been performed but will be in the near future.

Discussion

DR. JACK WOLF: I agree with the diagnosis of verrucous nevus. It is not an uncommon lesion in this location. These lesions may be smooth during the first few years of life and then tend to become verrucous. I have never seen this type of lesion become malignant, but the literature states that they occasionally do go on to malignant transformation. To avoid the trauma produced by the teeth of the comb, I use trichloracetic acid to remove the verrucous aspect and bring the lesion to the level of the skin surface.

DR. A. C. CIPOLLARO: I agree with the diagnosis of verrucous nevus of the scalp. However, there are some features which suggest sebaceous nevus. Squamous-cell epithelioma occasionally develops in sebaceous nevus.

DR. G. F. MACHACEK: The color suggested the possibility of its being sebaceous nevus. I think an absolutely curative therapy would be to excise the lesion and to undermine and oppose the edges. The thin scar would be covered by hair.

DR. M. J. COSTELLO: I agree with Dr. Cipollaro that it is a sebaceous nevus, and if the larger lesions are neglected they develop a foul-smelling sebaceous secretion. When smooth, they suggest minor ectodermal defects which occur in the same location. If this were my patient, I would treat the lesion by fractional doses of refrigeration with carbon dioxide snow. I think that would give a good result.

DR. J. W. DOUGHERTY: In the clinic we had a case similar to this which proved to be a sebaceous nevus with a basal-cell epithelioma. We excised it serially and got a good result; only a thin line was left. We waited two or three months between each excision.

DR. WILBERT SACHS: I agree with everybody. I think it is a sebaceous nevus, and I wonder whether simple treatment would get rid of it. If this is a combined nevus it goes deeper, as Dr. Machacek said, and you may have to go very deep to remove it. I doubt seriously whether this lesion will ever become malignant.

DR. DAVID BLOOM: The appearance is typical of a verrucous nevus on the scalp. Sebaceous nevus is more yellowish in color and softer in consistency. I feel certain that a biopsy specimen will confirm this diagnosis.

DR. WILBERT SACHS: If there were an associated fibromatous lesion you wouldn't see the yellow color.

DR. PAUL GROSS: In this nevus one should not take anything for granted, as Dr. Sachs said. Only a biopsy can decide whether it is a verrucous or a sebaceous nevus or whether some elements of syringocystadenoma papilliferum are present. Only the sebaceous glands and sweat gland elements in these nevi may give rise to epithelioma.

DR. M. J. COSTELLO: This patient said the lesion was smooth at first and later became verrucous. A verrucous nevus is verrucous from the start. A biopsy will settle the question.

Lichen Striatus. Presented by DR. JOHN W. DOUGHERTY.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Maurice M. Tolman, M.D., President

Paul J. Catinella, M.D., Secretary

Dec. 4, 1957

Erythema Induratum (Erythema Nodosum)?
Presented by DR. A. A. SOIFER.

A Portuguese woman aged 26 has had an eruption on the back of the legs since 1950. She was exposed to tuberculosis through her grandfather, who died of the pulmonary form of the disease.

At the age of 2 the patient's cervical nodes abscessed and drained. A node was removed, "diagnosis unknown." In the spring of 1950 several nontender indurated spots were noted on both legs. These disappeared after penicillin therapy but reappeared the following winter. There have been recurrent lesions since that time. In 1953 the patient noticed about 30 new lesions on the back of her legs, which she treated with ultraviolet light; these subsequently became more tender and ulcerated. By July, 1953, all lesions had healed, leaving depressed scars. There was a recurrence in October, and others have occurred intermittently since, but the lesions have not ulcerated since 1954. The patient believes that the lesions appear or become worse during her menstrual periods. She was studied at the Lahey Clinic and at the Massachusetts General Hospital, where she worked in 1954.

On the right leg there are several nontender, semifirm, subcutaneous nodules on the medial-posterior aspect of the middle third, and depressed

Submitted for publication May 6, 1958.

scars from previous lesions are seen. The left leg is free except for scarring.

Several roentgenograms of the chest have been normal or have shown healed tuberculosis.

Biopsy of a specimen from the left leg, removed at Massachusetts General Hospital on Jan. 7, 1954, was reported as showing "no diagnostic abnormality."

A tuberculin test on that date with second-strength purified protein derivative injected intracutaneously was strongly positive after 24 hours. Culture from an ulcer in May, 1953, yielded Micrococcus pyogenes. The Hinton reaction was negative, and the urine, stool, and sedimentation rate were normal.

Treatment in 1954 consisted of dihydrostreptomycin and PAS tablets, estrogens, and androgens. Since 1957 she has been given isoniazid, 400 mg. daily, pyridoxine, Gantrisin, and Calciferol, 200,000 units daily. Treatment has not influenced recurrences.

Discussion

DR. E. MYLES STANDISH: I don't know the diagnosis. It might be better classified in the vasculitis group. I have seen a number of cases of erythema nodosum which have ulcerated. These lesions are in the area affected by erythema induratum, and with a history of exposure to tuberculosis and a positive tuberculin test, I believe, it is too bad that the inoculated guinea pig was lost. This should be rechecked if possible. She states that she gets relief when the leg is elevated. In the few vasculitis cases I have seen, that is not necessarily the case. They usually get relief by motion and by using a supportive bandage or a gelatin cast. That is a suggestion for treatment.

DR. MAURICE M. TOLMAN: The question arises of where in the pigeonholes of tuberculosis erythema induratum belongs. Is it tuberculosis cutis in the true sense, or is it a tuberculid by definition? Very few instances of erythema induratum have been proved to have the tubercle bacillus in situ, and the guinea-pig inoculations that become positive are few and far between. They do not have the caseation type of pathology, and they do not respond anywhere nearly as well to the streptomycins, to isonicotinic acid hydrazide, or to the various other newer drugs as do the other types of tuberculosis. Therefore, I think it is erroneous to speak of this as tuberculosis, by modern standards. Standards in the old days were another story. We do not know their basis of nutritional values or other factors that came into play. With modern nutritional and other standards, and with modern antibiotics, so-called paratuberculosis as it was seen in the old days has been eliminated.

DR. JOSEPH MULLER: From the clinical picture alone I consider this a case of tuberculosis rather than of vasculitis. This type of case was rather common in Europe a good many years ago. I have seen only one case resembling this in all my 35 years here where I was able to culture the tubercle bacillus. I do think it would be advisable to get more guinea-pig inoculations, and for treatment surgical drainage and the usual after-care should give good results. I don't think dermatologists are unanimous about acknowledging erythema induratum as tuberculosis. I should say the pathologic picture of these lesions would rather resemble that of scrofuloderma in the old-fashioned terms. I did not use the current terminology for the simple reason that I don't think I have seen a case of cutaneous tuberculosis in the last 15 years, and I am more familiar with the old terminology.

DR. ALFRED HOLLANDER: I believe it is important to recognize erythema induratum of Bazin as a clinical entity and to differentiate it from erythema nodosum. The location of subcutaneous nodular lesions predominantly on the posterior aspect of the legs, the chronicity and at times ulceration of the lesions are important features in the diagnosis of erythema induratum of Bazin. In classification, it is best to follow the scheme of Jadassohn and Lewandowsky. Erythema induratum is classified as tuberculosis cutis indurativa.

DR. EDWARD A. LEFRENIERE: I recall a case of erythema induratum of the leg proven by biopsy, in which the patient had no evidence of tuberculosis anywhere. She had scars on the legs, and plastic surgery was performed. The graft on the right leg was larger than the size of a palm, and it was taken from the abdomen. She developed new lesions in the skin graft without having lesions in the abdomen or anywhere else, then or in the past.

Urticaria Pigmentosa (Telangiectasia Macularis Eruptiva Perstans). Presented by DR. CHARLES S. D'AVANZO.

A white school boy aged 11 has had a generalized eruption for nine weeks. It began on the chest, and the parents state that after a polio injection the eruption got worse and became generalized. The patient also felt ill for one day and had symptoms resembling a cold. The parents say he has been more irritable since the eruption developed.

The face, neck, eyelids, trunk and, upper and lower extremities show numerous discrete, pinhead- to pea-sized petechial lesions. These are most numerous on the upper and lower extremities. Urtication can be produced on some of the macular lesions by rubbing.

On microscopic examination the vessels of the corium showed a moderate infiltration of lymphocytes and spindle-shaped cells which on Giemsa staining showed metachromatic granules. There appeared, therefore, to be an increase in the number of mast cells.

The Hinton reaction was negative, and urinalysis was normal. The hematocrit was 38%; hemoglobin, 12.6 gm., and white blood cells, 3900, with polymorphonuclear leukocytes 47%, lymphocytes 40%, monocytes 9%, eosinophils 2%, and band forms 2%. The platelet count was 140,000.

Biopsy (Dr. Margaret Gray Wood) showed histopathologic findings compatible with the inflammatory type of urticaria pigmentosa.

Three weeks later (Nov. 30, 1957) the hemoglobin was 12.6 gm., hematocrit 38%, and white blood cells 8450, with polymorphonuclear leukocytes 43%, lymphocytes 47%, monocytes 8%, and eosinophils 2%. The red blood cells were normal, and platelets appeared adequate on stained smear.

The bleeding time was 2 minutes 30 seconds (normal: 1 to 3 minutes); clotting time, 12 minutes 30 seconds (Lee-White normal: up to 14 minutes); platelet count 226,000 (normal: 250,000 to 350,000).

Clot retraction studies: 1-hour report, clot had not yet started to retract (normal: complete retraction in 24 hours); 24-hour report, clot was very slightly retracted and the serum volume was greatly decreased. The clot was very soft and boggy and flattened out as a shapeless mass from which serum continued to drain.

Capillary fragility studies: Before application of blood-pressure cuff there were 13 petechial hemorrhages in an area of 5 sq. cm. After seven minutes' pressure the cuff was released, and five minutes later petechial hemorrhages in the same area numbered 33 (normal: 10-20).

Discussion

DR. MAURICE M. TOLMAN: I believe we are dealing with a case of pityriasis lichenoides. The eruption came on rather acutely, and the patient said there was no itching at all. There seemed to be a few excoriated little papules. These papules were discrete and several seemed to have a hemorrhagic center, as though there might have been a vesicle there at one time. I asked if he had ever had tiny blisters and he said he had. Whether that was an answer to a leading question, I don't know.

DR. ALFRED HOLLANDER: When Dr. D'Avanzo showed me this patient several weeks ago, I felt acute parapsoriasis had to be considered. Today it is not difficult to make a clinical diagnosis of acute parapsoriasis (pityriasis lichenoides et varioliformis acuta of Mucha-Habermann). Dr. D'Avanzo also considered parapsoriasis, but the histologic report made him change the diagnosis. As for treatment, I feel this case should be left alone.

DR. A. A. SOIFER: Since urticaria pigmentosa is not limited to the skin, I suggest a roentgenogram of the bones.

DR. CHARLES S. D'AVANZO: When I saw this patient about a month ago the picture was quite different. He then had many more lesions on the trunk and neck, and there were distinct, brown, pea-sized, flat, macular lesions besides those he now has on the arms and legs, and he had many petechial lesions that did not blanch out at all. He has some petechial lesions at this time. When macules on the chest were rubbed, some of them appeared to rise up. A biopsy was performed at that time, and a tentative diagnosis of acute parapsoriasis was made with a question mark, along with an unusual type of urticaria pigmentosa or an unusual purpura. These were the three diagnoses considered. The patient was presented under the diagnosis of urticaria pigmentosa because of the histologic report. However, the picture has changed. The blood shows definite changes, and exactly what that means I do not know. There is something wrong with the clot retraction time, there is increase in the capillary fragility, and there seems to be something wrong with the platelets. I am not entirely satisfied with the diagnosis of acute parapsoriasis, although that was also my first diagnosis. The pathologist made me swing a little more to an acute telangiectatic type of urticaria pigmentosa.

Case for Diagnosis: Hypertrophic Lichen Planus; Neurodermatitis? Presented by DR. BERNARD APPEL.

Nummular Eczema. Presented by DR. WILLIAM WOLF.

Discoid Lupus Erythematosus. Presented by DR. E. FINNERTY.

Case for Diagnosis: Alopecia Totalis; Vogt-Koyanagi Syndrome? Presented from BOSTON CITY HOSPITAL.

Case for Diagnosis: Neurodermatitis? Presented by DR. DAVID FOLAN JR.

Lichen Planus. Presented by DR. BERNARD APPEL.

Pigmented Purpuric Lichenoid Dermatitis. Presented by DR. BERNARD APPEL.

Ainhum. Presented by DR. BERNARD APPEL.

Pemphigus Vulgaris, Under Control. Presented by DR. DAVID W. FOLAN JR.

Keratosis Pilaris; Linear Nevus of Upper Extremities. Presented from BOSTON CITY HOSPITAL.

Generalized Herpes Zoster: Cancer of Sigmoid, Postoperative. Presented by DR. BERNARD APPEL.

Case for Diagnosis: Neurodermatitis; Keratosis Follicularis? Presented by DR. WILLIAM WOLF.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. G. ROBERT BALER.

Scleroderma (Aerosclerosis) Response to Steroids. Presented by DR. A. A. SOIFER.

Hypertrophic Lichen Planus (Legs): Chronic Recurrent Lichen Planus of Trunk and Extremities; Dermatitis Herpetiformis? Presented by DR. A. A. SOIFER.

Pseudopelade. Presented by DR. WILLIAM WOLF.

Case for Diagnosis: Kaposi's Sarcoma; Fixed Drug Eruption; Arteriovenous Aneurysm; Circumscribed Neurodermatitis? Presented by DR. ALBERT A. SOIFER.

NEW YORK DERMATOLOGICAL SOCIETY

J. Lowry Miller, M.D., President

Frank E. Cormia, M.D., Secretary

Nov. 26, 1957

Chromoblastomycosis Occurring in New York City. Presented by DR. MAURICE J. COSTELLO.

A 47-year-old Negro is presented from Lenox Hill Hospital, where he was found to have pulmonary sarcoidosis on routine preemployment roentgenography of his chest. At that time it was noted that he had a palm-sized granulomatous lesion on the right ankle, which began eight years ago when he struck this area with an ax while chopping wood. This lesion had a raised border, a central fissured area, and surrounding mottled, macular hyperpigmentation. No similar lesions were detected elsewhere. He had a history of contact with tuberculosis in his youth. There were bilateral corneal opacities, worse on the right side, which prevented him from reading ordinary print. The loss of visual acuity was greater in the right eye than in the left. This probably represented an old interstitial keratitis of congenital syphilis, since his Wassermann reaction is still weakly positive.

The following tests were negative: tuberculin, histoplasmin, coccidioidin, blastomycin, Kveim. The blood count was normal. Examination and culture of the sputum were negative for acid-fast bacilli.

Liver biopsy did not show sarcoidosis.

Blood chemistry examinations were as follows:

Blood calcium	10.8
Erythrocyte sedimentation rate	87 mm. in one hour
Urea nitrogen	11.3 mg/100 cc.
Glucose	103.0 mg/100 cc.
Hematocrit	43.3
Total proteins	6.6 gm.
Albumin	2.8 gm.
Globulin	3.9 gm.

An electrocardiogram showed a sinus bradycardia with a right bundle branch block.

On roentgenography the pulmonary field showed bilateral hilar adenopathy and mottled infiltration of both lung fields, quite severe in the upper lobes, without cavitation. There was no evidence of pleural involvement.

The conclusion was sarcoidosis, as most likely.

A biopsy was obtained by lifting out a pea-sized, moist, rounded body which histologically showed a granuloma studded with chromoblastomyces. There were classical, sclerotic, rounded, budding bodies which were both single and grouped, with a chestnut discoloration.

The culture, presented here, was grossly suggestive of Hormodendrum and Phialophora.

Submitted for publication April 29, 1958.

We expect to have in vitro studies and sensitivity studies performed to determine whether Amphotericin B will be effective.

X-ray therapy has been administered with improvement.

Discussion

DR. A. C. CIPOLLARO: I would have missed the diagnosis in this patient, and I wouldn't even have thought of doing a culture. I wonder how many of these cases we are missing. Last week I had a letter from Dr. Edward Abbey, of Fort Lauderdale, saying that he had a case of chromoblastomycosis. Evidently it is not confined altogether to the equatorial region.

DR. FRANK E. CORMIA: We presented a case of chromoblastomycosis a few years ago, and it is my impression that it originated in New York City. Perhaps Dr. Lewis will recall the case.

DR. GEORGE M. LEWIS: The culture certainly suggests Hormodendrum pedrosoi, confirming nicely the studies already made and the histologic sections. Clinically, it is more than just a simple scaling or low-grade inflammation. There is some evidence that it is a deep process, confirmed by the slide and now by the culture.

DR. WILBERT SACHS: To my knowledge, this is the first case of chromoblastomycosis that originated in this city. Histologically, it was a very deep process in Dr. Lewis's case on the hand. The little granules came out in three different colors. My diagnosis when I saw the patient at City Hospital was maduromycosis.

DR. MAURICE J. COSTELLO: This man has pulmonary lesions suggestive of sarcoidosis, but the Kveim test was negative and the liver biopsy, which I believe is positive in 80% of cases of sarcoidosis, was also negative. When I learned he had lesions in the lungs, my purpose was to prove that the lesion on the leg was also sarcoid. However, the pulmonary lesions may be a sarcoid-like reaction to chromoblastomycosis. Such an experience has never been reported.

Leiner's Disease; Treated with Biotin. Presented by DR. LESLIE P. BARKER.

A baby girl, white, aged 9 weeks, developed a dermatitis of the diaper area at the age of 4 weeks. The eruption spread to include the face, scalp, neck, and, in a patchy fashion, most of the trunk. She had thrush in the mouth at the age of 2 weeks, and this was cured with gentian violet. There were no gastrointestinal symptoms.

The baby has been bottle-fed since birth and takes the formula well. This consists of evaporated milk with added vitamins.

When the mother was seven months pregnant she had "flu," for which she was treated with penicillin and Aureomycin for about 10 days.

Examination shows typical cradle-cap, with dermatitis of the face, neck, and diaper area. It is also seen in patchy distribution over the entire trunk. The involved areas are covered with yellowish, greasy, scales.

Treatment has consisted of injections of biotin, 10 mg. three times weekly. Locally, only olive oil has been used to cleanse the skin.

Discussion

DR. GEORGE M. LEWIS: I will agree with the diagnosis. In spite of the history and the strong impression of Dr. Barker that biotin has been responsible for the improvement, I doubt that such is the case. Biotin has been extensively assayed without any value demonstrated in this type of case.

DR. FRANK C. COMBES: The improvement in this case, if it can be attributed to biotin, and I think it can, is remarkable. As Dr. Lewis says, it is not used in dermatology. I wonder whether the same effect couldn't be obtained by injections of pyridoxine hydrochloride.

DR. HERBERT KRAUT (by invitation): I have seen the patient at the hospital, and I, too, wondered whether the biotin accomplished anything, so I asked the mother whether those areas of the body to which the ointment was not being applied had improved as well, and she said they had. The only treatment they were getting was the biotin systemically.

DR. FRANK E. CORMIA: I think Sebrell was one of the first to point out that humans on biotin deficiency developed seborrhea-like eruptions. Dr. Oppel worked with biotin and he found that it was of no value in the treatment of seborrheic dermatitis. However, I would still keep an open mind about the improvement Dr. Barker has reported. I wonder whether there is any local effect, because I think biotin has to be absorbed parenterally.

DR. LESLIE P. BARKER: Biotin alone, or in combination with vitamin B complex has been used many times for the treatment of Leiner's disease with good to excellent results. These infants are very susceptible to skin infections, and antibiotics, locally or systemically, are often required to control the secondary infection. Leiner's disease most frequently occurs in breast-fed babies in countries where the diet is poor in vitamins. Both the mothers' and the infants' bloods were found to be low in biotin. Sydenstricker was able to produce a seborrhea-like eruption in humans by feeding a biotin-free diet and giving raw egg-white to further prevent absorption of biotin. These volunteers promptly recovered when given injections of biotin.

DR. FRANK E. CORMIA: Sydenstricker and Sebrell worked together in the study of biotin deficiency. Did these children get eggs?

DR. LESLIE P. BARKER: These infants had not received eggs, and only raw egg-white prevents the absorption of biotin.

Probable Systemic Lupus Erythematosus. Presented by DR. CARL T. NELSON.

A white housewife aged 38 was in relatively good health until about ten years ago, when she developed intermittent migratory arthralgia. This was considered to be mild rheumatoid arthritis. Approximately four years ago, following her fifth spontaneous abortion, it was noted that she had characteristic murmurs of rheumatic heart disease but no symptoms or history thereof. Four years ago she noted weakness and numbness in the left ankle, and this has continued. One year ago she was found to be hypertensive. Since 1954 there has been a gradual increase in numbness, easy fatigability and weakness, with involvement of the hands as well as the feet. For the past year a blotchy erythematous eruption has been present on the hands and forearms. This has been associated with numbness and blanching on exposure to cold. The patient has also noted a tendency to bruise easily for the past several months.

The malar areas of the face reveal slight erythema and numerous telangiectases, but no scaling or atrophy. The distal surfaces of the upper extremities show a livedo-like, reticulated, mottled discoloration. The digits show moderate clubbing, cyanosis, and fine telangiectases at the base of all nails.

Laboratory examinations:

Hemoglobin	16.5 gm/100 cc.
White blood cells	7600 (N-63;E-3; B-1; L-32; M-1)
Urinalysis	2+ albumin—otherwise normal
ESR	19 mm. in an hour
Serologic tests for syphilis	Positive
Treponema pallidum immobilization test	Negative
Cephalin flocculation	3+
Thymol turbidity	2+
L. E. preparation (one)	Negative
Serum proteins	6.9 gm. % (alb. 4.7 gm. %, glob. 2.2 gm. %)
Electromyogram	Normal
Bleeding time	6 minutes 20 seconds
Clotting time	4 minutes 15 seconds
Prothrombin time	17 seconds (normal: 15 seconds)
Cryoglobulins	Positive in moderate amounts

Discussion

DR. LESLIE P. BARKER: I saw this patient when she was admitted to the clinic. The marked redness and telangiectasia around the base of the nails, the cold hands and feet with mild reticulated erythema of the extremities, would suggest a collagen disease, particularly lupus erythematosus.

DR. FRANK C. COMBES: I agree with the diagnosis of possible lupus erythematosus. I think most of the symptoms, though, might be explained otherwise. The patient has a lot of cyanosis, particularly of the fingernails, which might be due to cardiovascular disease of other cause. The diagnosis of systemic lupus erythematosus is extremely difficult in the absence of cutaneous lesions, as in this case, and of L. E. cells, leukopenia, etc., which this patient does not show. I don't know what the sedimentation rate was, but it wouldn't matter much because you could get an elevated rate from other causes. I would examine the eyes. Exudative retinitis is not at all uncommon in subacute systemic lupus erythematosus.

DR. MAURICE J. COSTELLO: I would agree with the diagnosis as presented. I think ample evidence has been given certainly to more than suggest that diagnosis. Out of six pregnancies the patient has had five spontaneous abortions. Incidentally, until recently I hadn't seen Raynaud's phenomenon associated with systemic lupus erythematosus. Clubbing of her fingers should suggest further examinations of the heart. In addition to the 2+ albumin in the urine, etc., I don't know what more one needs to make a diagnosis of systemic lupus erythematosus. I think cytoid bodies are worth looking for.

DR. FRANK E. CORMIA: As Dr. Combes and Dr. Costello have pointed out, the most probable diagnosis is lupus erythematosus. However, I wonder whether or not the cryoglobulins may not have a good deal to do with the peripheral vascular lesions. Furthermore, it is unusual to see systemic lupus erythematosus with active manifestations in the extremities without finding L. E. cells.

DR. CARL T. NELSON: This is really a case of cryoglobulinemia. The cyanosis, the livedo-like lesions of the extremities, and the sensitivity to cold can be explained on that basis. Presumably this patient has symptomatic cryoglobulinemia; hence, we are looking very hard for an abnormal underlying condition that might be responsible for it. Lymphoma, liver disease, subacute bacterial endocarditis, and multiple myeloma do not seem to be pertinent to this case. Actually, we believe that this patient has systemic lupus erythematosus, although cryoglobulinemia is only infrequently associated with that disease. In answer to some of the questions raised, the ophthalmologists have examined the patient by slit lamp and there are no retinal lesions or cytoid bodies. Certainly she has mitral heart disease, with systolic and diastolic murmurs. I wonder whether this may not be part of the so-called Libman-Sachs syndrome. I agree with Dr. Costello that the patient has enough cardiac abnormalities to account for some of the clubbing and cyanosis. Only one L. E.-cell determination has been done, and this was negative. In the hospital the patient has deteriorated rapidly mentally; she is forgetful and cannot find her way around the wards. Whether that goes with the general possibility of collagen disease is a moot point at this time.

DR. MAURICE J. COSTELLO: Is there any possibility of polycythemia?

DR. CARL T. NELSON: No, there were 4,000,000 red cells with a high hemoglobin. The sedimentation rate is normal. There are several things against a diagnosis of lupus erythematosus.

DR. FRANK E. CORMIA: The cerebral symptoms are suggestive of lupus erythematosus.

Secondary Syphilis with Alopecia. Presented by DR. FRANK E. CORMIA.

A generally healthy Negro man aged 26 has had several unprotected sexual exposures in the past six months. A primary lesion was not noted. A rather diffuse loss of scalp hair has occurred in the past three and one-half weeks. On Nov. 15 the Mazzini reaction of the blood was positive in a dilution of 1:32. There were no other symptoms. Physical examination, including anoscopy, was normal with the exception of scattered doughy adenopathy.

There is a moth-eaten type of alopecia on the scalp, most marked in the posterior portion. The lower part of the soft palate shows dusky red inflammation. A scattered, doughy adenopathy, including the epitrochlear glands, is present. There is no eruption on the body.

Discussion

DR. GEORGE M. LEWIS: The clinical features favor the diagnosis. It will be interesting if the biopsy findings show enough plasma-cell infiltration to account for the alopecia. This man is both heterosexual and homosexual.

DR. MAURICE J. COSTELLO: I think Dr. Lewis has given one of the reasons why the original lesion was not found. It may have been anorectal, anal, or possibly on his tonsil.

DR. FRANK E. CORMIA: Dr. Dougherty, who first saw the patient in the clinic, had an anoscopic examination performed, and no chancre was found. I must confess I was greatly remiss in performing

my examination. I saw the patient briefly at our conference, looked in his throat, saw the more or less typical infiltration in the palate, but missed the enlargement of the tonsils. I believe the patient has secondary syphilis of the tonsils, as well. Over the years I have seen but few patients with secondary syphilis of the tonsils. In the few I have observed with a primary tonsillar lesion, it was always unilateral.

Junction Nevus. Presented by DR. MAURICE J. COSTELLO. (Previously presented before Manhattan Dermatological Society Nov. 12, 1957.)

Granuloma Annulare. Presented by DR. FRANK E. CORMIA.

Congenital Ichthyosiform Erythroderma. Presented by DR. LESLIE P. BARKER.

Pityriasis Rubra Pilaris: Acute Acquired Type, Showing Response to Steroids. Presented by DR. L. P. BARKER.

Lichen Planus, Limited to the Mouth. Presented by DR. LESLIE P. BARKER.

Abstracts from Current Literature

Effect of Chemical Substances on T. Mentagrophytes by Use of Infected Guinea Pig Hairs (Hair Test). P. Wenk and J. R. Frey, Arch. klin. u. exper. Dermat. 207:1-23 (April) 1958.

The course of infection and the localization of fungous elements in the hair of guinea pigs infected with T. mentagrophytes was studied in order to determine the effect of various chemical substances (Asterol and others). Localization of fungous elements in the hair of infected guinea pigs was similar to that of human hair in tinea capitis as described by Kligman. Chemical substances which prevent the development of cultures from infected hair after four-hour contact are called hair-test active. They destroy peripilary spores only, but not intrapilary hyphae. Hair-test-inactive substances do not destroy peripilary spores even if exposed apart from hair (spore suspension test). By destroying peripilary spores, hair-test-active substances cannot cure tinea. They may prevent the formation of new foci and the spreading of the infection to other persons.

Hollander, Springfield, Mass.

Investigations on Saprophytic Dermatophytes in Soil. B. Ettig, Arch. klin. u. exper. Dermat. 207:24-33 (April) 1958.

Fifty bacteria and Actinomyces of various sorts were isolated from soil and were grown on yeast peptone agar, malt extract peptone agar, and Waksman's starch agar. The antibiotic effect of active bacteria and Actinomyces on M. gypseum, E. floccosum, T. rubrum, and T. mentagrophytes was examined. Some bacteria and Actinomycetes had an antagonistic influence in vitro on the tested dermatophytes. Antibiotic inactivity was also observed. Some bacteria were overgrown by the tested fungus; some Actinomyces had a synergistic influence on fungi.

Hollander, Springfield, Mass.

Multiple Ganglioneuromas. F. Nödl, Arch. klin. u. exper. Dermat. 207:46-62 (April) 1958.

According to the author, the following case represents the third in the literature. Multiple ganglioneuromas developed on the back of a baby girl, beginning with the 9th month of life. An erroneous clinical diagnosis of lipoma was made. With the aid of silver impregnation it could be shown microscopically that the tumors contained nerve fibers of various thicknesses and nerve cells originating from the sympathicus. Histogenetically, the development of fibrous nerve tissue preceded the appearance of ganglion cells. The clinical and histologic differences of tumors described as ganglioneuromas which really are reticulohistiocytomas abundant with giant cells are discussed.

Hollander, Springfield, Mass.

Tinea Epidemic in Kaiserslautern Caused by Microsporum Canis and Transmitted by Cats. W. Kiessling, J. Schönfeld, and E. Bender, Arch. klin. u. exper. Dermat. 207:71-85 (April) 1958.

This is a report of the first observation in Germany of a tinea epidemic due to M. canis with simultaneous findings in cats. The infection was recognized in 15 children and 1 adult living in the same quarters in Kaiserslautern. The source of contagion was cats. Clinically, under Wood's light, microscopically, and by culture infection due to M. canis was proven in one cat. Local treatment was successful in all cases within a short period of time.

Hollander, Springfield, Mass.

"Trichoadenoma" (Organoid Hair Follicle Hamartoma). W. Nikolowski, Arch. klin. u. exper. Dermat. 207:34-45 (April) 1958.

A 63-year-old man had for 15 years a slowly growing pea-sized cutaneous nodule of the flexor aspect of the right thigh. The lesion protruded in semiglobular form. Histologically, the cutis showed two distinctly separated groups of cysts filled with keratin lamellae and solid round-cell complexes. The lining of these formations consisted of basal- and prickle-cell types. Some of the cells contained keratohyalin granules. There also were translucent cells like those

found in the stratum lucidum. The author feels that owing to the finding of prickle cells the tumor should be classified as organoid hair follicle hamartoma.

HOLLANDER, Springfield, Mass.

VITAMIN A IN INFLAMMATORY DERMATOSES AND THOSE WITH DISTURBANCES OF KERATINIZATION. P. ZIERZ, M. TAUGNER, and G. BRAXMAIER, Arch. klin. u. exper. Dermat. 207:86-98 (April) 1958.

Examinations are presented of 90 patients with psoriasis vulgaris, acne vulgaris, alopecia areata and totalis, and lichen chronicus Vidal and 42 patients with diseases such as ulcus cruris, mycotic eczema, and gonorrhea. The latter group comprised diseases in which there is a disturbance of vitamin A metabolism. This control group showed in 76% fasting values of vitamin A serum concentration between 150 and 300 I. U. In psoriasis, acne, and lichen Vidal there were values similar to the control group. One fourth of the cases of alopecias showed values below 150 I. U. Concerning the resorption of vitamin A, there was no difference in psoriasis as compared with the control group. Variations from the control group were found in acne, alopecia areata and totalis, and lichen Vidal. These variations did not allow any conclusions in regard to a causal relationship. The authors feel that there is no proven indication for vitamin A therapy in psoriasis. They recommend vitamin A therapy in acne vulgaris, alopecias, and lichen Vidal.

HOLLANDER, Springfield, Mass.

SUCCESSFUL TREATMENT OF ICHTHYOSIS CONGENITA GRAVIS WITH CORTISONE. H. HANSSLER, German Medical Monthly 3:33-45 (Feb.) 1958.

A 2-day-old baby suffering from ichthyosis congenita gravis was successfully treated with cortisone and vitamin A. Two siblings had died of the same disease shortly after birth. At the age of 18 months, one year after cortisone was discontinued, the treated child was found to be in normal physical and mental health.

BULEY, Champaign, Ill.

HISTOCHEMICAL FINDINGS OF ALKALINE PHOSPHATASE IN NORMAL AND DISEASED HAIR ROOTS. G. KLINGMÜLLER, Hautarzt 9:176-180 (April) 1958.

The histochemical demonstration of alkaline phosphatase shows remarkable differences in the morphology and fermentative functions of the capillaries and the follicles in the shedding of normal hair and that of the diseased hair in alopecia areata. The changes noted in alopecia areata, however, are probably not specific, and the interpretation of their significance is, as yet, only hypothetical.

BULEY, Champaign, Ill.

LIPOID GRANULOMATOSIS OF THE SUBCUTIS. H. LAUSECKER, Hautarzt 9:165-169 (April) 1958.

A case of subcutaneous lipoid granulomatosis with involvement of the lymph nodes, liver, and spleen is described. The histological sections of the lesions are characterized by a dense infiltrate of plasma cells surrounding the lipoid granulomas.

Considering the concept that plasma cells produce antibodies, the author suggests that the disease is the result of an infectious-allergic process in a constitutionally abnormal terrain.

BULEY, Champaign, Ill.

LYMPHADENOSIS BENIGNA CUTIS—A TRANSMISSIBLE INFECTIOUS DISEASE. J. M. PASCHOUD, Hautarzt 9:153-165 (April) 1958.

Material taken from secondary lymphadenosis benigna cutis of the ear lobe, experimentally produced by inoculation of material from an original case, was further inoculated into the skin over the right scapula of two volunteers. Within 11 weeks the clinical picture of erythema chronicum migrans with central lymphocytomas resulted in both cases.

BULEY, Champaign, Ill.

MYCOSIS FUNGOIDES AS A RETICULOSIS. K. STORDEUR AND F. KESSLER, Hautarzt 9:169-176 (April) 1958.

A case of mycosis fungoides, observed over a period of six years, is presented, and the autopsy findings are reported. The authors feel that mycosis fungoides is a neoplastic disease of the reticulohistiocytic system. The sarcomatous changes in internal organs should not be explained as metastases in the customary sense but rather as manifestations of a disease of multicentric origin in which the individual lesions attain different degrees of malignancy.

BULEY, Champaign, Ill.

SIMULTANEOUS INFECTION WITH TRICHOPHYTON RUBRUM AND TRICHOPHYTON VERRUCOSUM. H. RIETH and C. SCHIRREN, Hautarzt 9:180-183 (April) 1958.

The rare simultaneous infection of a young farm helper with both Trichophyton rubrum Castellani and Trichophyton verrucosum Bodin is reported. Since the patient was previously exposed to infection with Trichophyton verrucosum without developing clinical lesions, the authors theorize that the spreading infection of Trichophyton rubrum weakened the biological defense of the patient sufficiently to make invasion by the second organism possible.

BULEY, Champaign, Ill.

ADRENAL CORTICAL HORMONES AND THE FORMATION OF HISTAMINE AND 5-HYDROXYTRYPTAMINE. R. HICKS and G. B. WEST, Nature, London 181:1342-1343 (May 10) 1958.

The amounts of histamine and 5-hydroxytryptamine in the tissues of rats treated with cortisone and hydroxycortisone were found to be much lower than the levels in control tissues. Marked degranulation of skin mast cells without disruption of the cell membrane was observed. Deoxycorticosterone acetate, in contrast, did not lower the tissue levels of these amines nor did it alter the morphology of the mast cells. After depletion of histamine by polymixin B treatment, the recovery rate of the tissue histamine was also retarded by cortisone and hydroxycortisone. The mechanism of these effects may be due to a lowering of the activity of both histidine decarboxylase and 5-hydroxytrytophan decarboxylase by cortisone and other glucocorticoids. The tissue levels of histamine and 5-hydroxytryptamine may, thus, be controlled by the adrenal cortical hormone corticosterone.

J. J. SMITH JR., Miami, Fla.

Announcements

Annual Award in Dermatology (Psoriasis).—The Department of Dermatology, Baylor University College of Medicine, announces the Mr. and Mrs. J. N. Taub International Memorial Award for Psoriasis Research. This award was established by Carol and Henry J. N. Taub in honor of their grandparents, Mr. and Mrs. J. N. Taub. The establishment of this ten-year program carried with it the hope that this award will be the instrumentality by which a cure may be developed to alleviate one of the problems of mankind.

An annual award of $1000 for research on psoriasis is designated for the individual or group who has done the most outstanding investigative work in this field. Results of the research must have been presented before a dermatological medical society or published in one of the recognized medical journals. The name of any applicant for the award, together with supporting data, should be submitted for consideration by Dec. 1, 1958.

The recipient of the award will be determined by a committee composed of Drs. Marcus R. Caro, Edward P. Cawley, Arthur C. Curtis, Eugene M. Farber, John M. Knox, Aaron B. Lerner, and Carl T. Nelson. If in the opinion of the committee a given calendar year fails to reveal a deserving contribution, the award will not be given.

Address all communications to

JOHN M. KNOX, M.D.
Department of Dermatology
Baylor University
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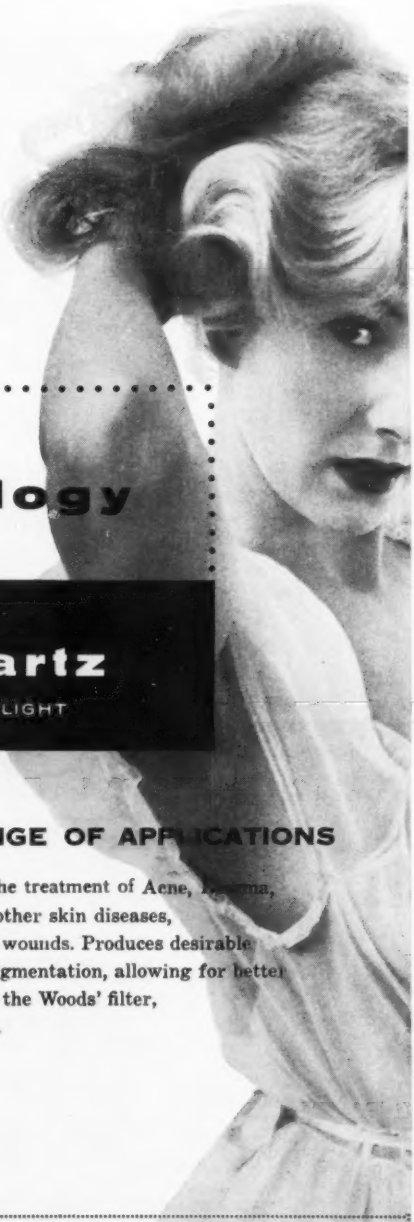
Houston 25, Texas

Labeling Hazardous Substances in Packaged Chemicals.—The growing demand for uniform legislation to require precautionary labeling of all chemical products, which are not now so regulated, was discussed at the first legislative conference held on May 9, 1958, at the American Medical Association Headquarters. Speaking to government, industry, and medical representatives from approximately 40 national organizations, members of the A. M. A. Committee on Toxicology discussed the "Uniform Hazardous Substances Act" and compared it with other tentative legislation which has been proposed.

Attention was focused on the general nature of the problem, as seen by the medical profession, public health officials, and the public, by remarks from a pediatrics representative, and officials of the American Public Health Association and the National Safety Council. The principles, which the Committee employed in formulating the provisions of a model law for labeling all types of hazardous substances, were next reviewed. A comparison of the model bill with other tentative legislative proposals followed.

An industry-wide label law conference was held on July 25, 1958, under the sponsorship of the Committee on Toxicology. The second meeting discussed proposed legislation requiring the declaration of hazardous ingredients and warning statements on the label and in the accompanying literature of household, commercial, and industrial packaged chemicals. Over 100 organizations, including representatives of trade associations, toxicity testing laboratories, chemical trade unions, and other interested groups, were invited to participate.

This was the second of several meetings which will be held to discuss proposals for local and federal regulations to close the gap in label legislation. A Committee survey showed a sketchy, nonuniform, and generally inadequate pattern of labeling regulations at the state and national level. Ninety per cent of the states lacked requirements for precautionary labeling of commercial as well as household chemical products. These meetings were held to bring about a clearer understanding of what the model bill is intended to cover and the benefits to be derived from such legislation.



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*Miller, J. M.; Godfrey, G. C.; Ginsberg, M., and Papastrat, C. J., in Surgical Service, V. A. Hospital, Fort Howard, Maryland: Postgrad. Med. *22*:609, 1957.

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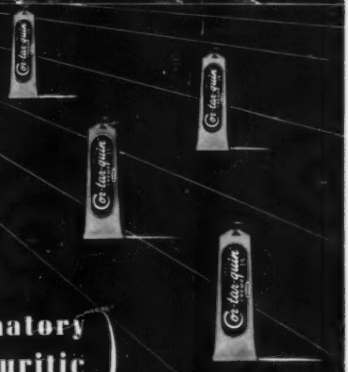

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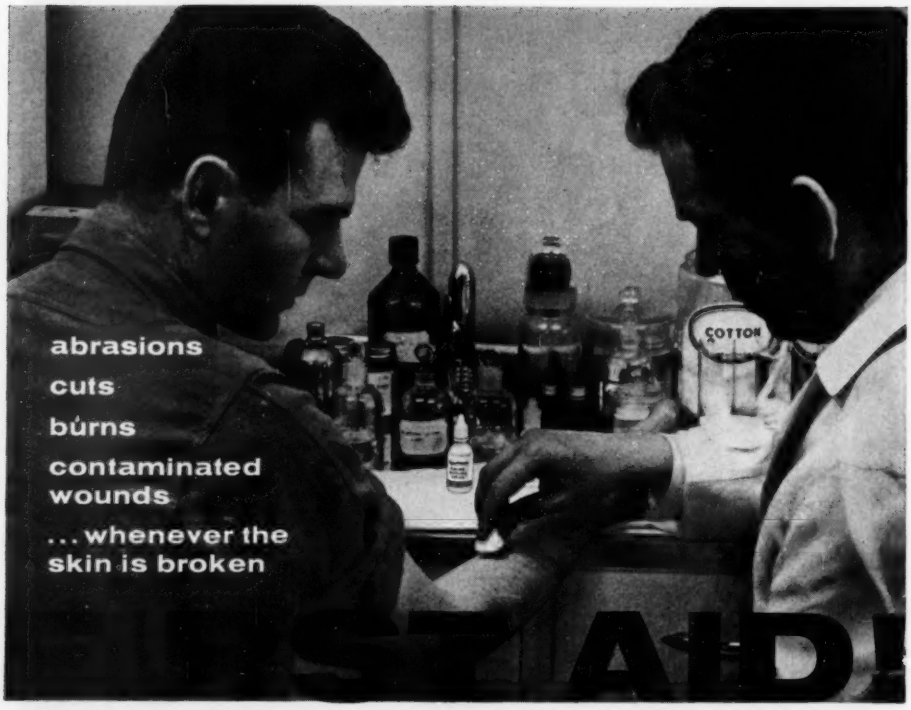

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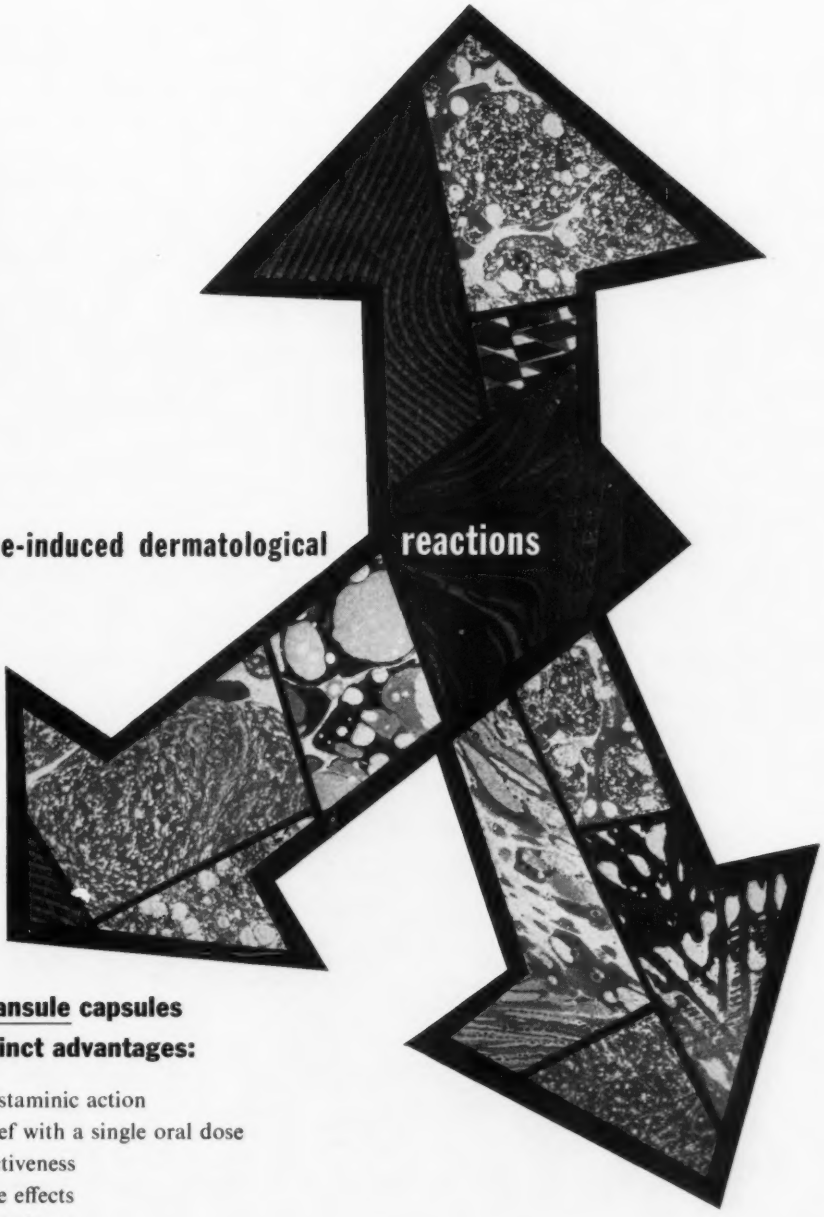

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Reference: Gross E. R. and Wright C. S., A. M. A. Archives of Dermatology, 78:92, July, 1958

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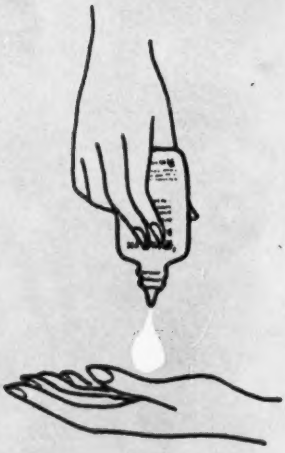

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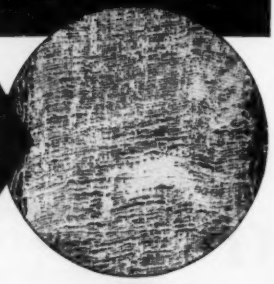

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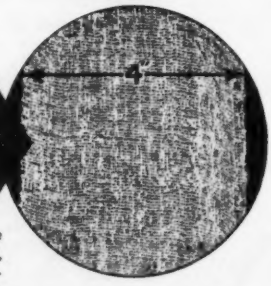

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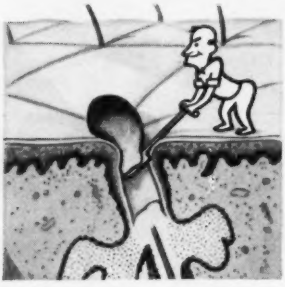

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—Gross, P., et al.: A. M. A. Arch. Dermat. & Syph. 70:94,1954.

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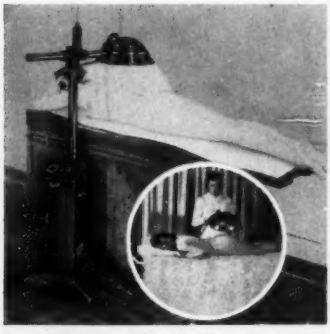

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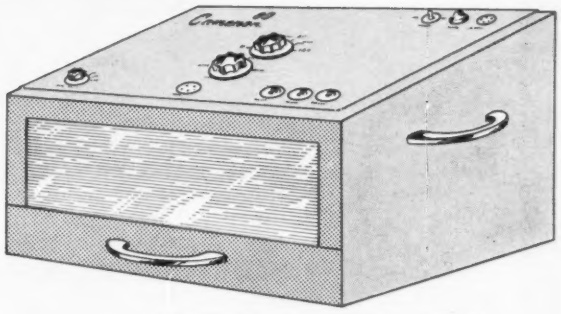

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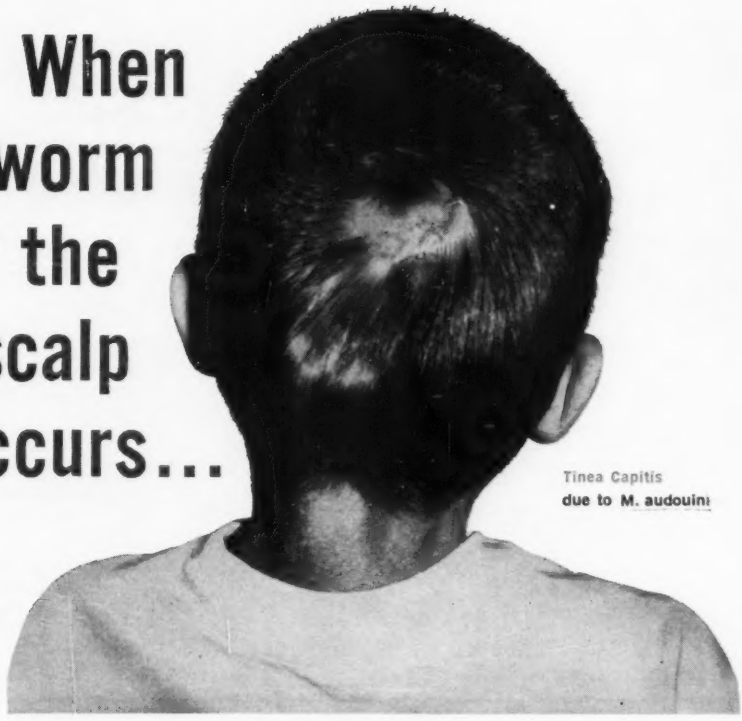

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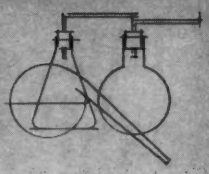

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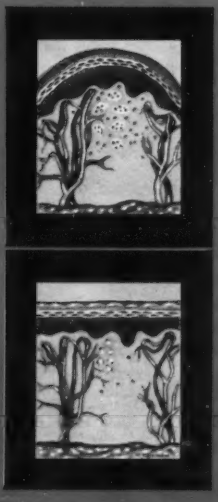

1. Welsh, A. L., and Ellis, M.: J.A.M.A. 160:158, 1956.

Additional Clinical Publications on Tarcortin:

Clyman, S. G.: Postgrad. Med. 21:309, 1957 • Bielberg, J.: J. M. Soc. New Jersey 53:37, 1956 • Abrams, B. P., and Shaw, C.: Clin. Med. 3:439, 1956 • Bielberg, J.: Am. Practitioner 6:1404, 1955

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1. Wiener, K.: Systemic Associations and Treatment of Skin Diseases, St. Louis, The C. V. Mosby Company, 1955, pp. 329; 458-459.
2. Perry, D. J.; Mount, G. D., and Browne, B. W.: The Effect of Varying Oral Dosages of Banthīne, Pro-Banthīne and Prantal on the Galvanic Skin Response, J. Invest. Dermat. *28*:239 (March) 1957.
3. Olansky, S., and Callaway, J. L., in Modern Medicine 1958 Annual (Part 1): Management of Superficial Infections, Minneapolis, Modern Medicine, 1957, p. 46.

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1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

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